104042

SEARCH REQUEST FORM
Scientific and Technical Information Center

Examiner : MARK HAN
Art Unit : 3763
Phone Number: 703-308-4543
Date: 16 SEPTEMBER 2003
Serial Number: 10/035,389
MailBox & Bldg/Room Location: CP2-3D16
Results Format Preferred (circle): Paper Disk E-mail

SEP 16 2003

If more than one search is submitted, please prioritize searches in order of need.
****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: *Methods and Apparatuses for Drug Delivery to an Intravascular Occlusion*

Inventors (please provide full names): GHOLAM-REZA (← first name) ZADNO-AZIZI (← last name)

Earliest Priority Filing Date: 23 JUNE 1998

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Claim 1: A method for treating an intravascular occlusion, comprising the step of delivering fluid containing an occlusion-treating drug such that at least a portion of the drug contacts an intravascular occlusive device.

Claim 2: The method of claim 1, wherein the occlusive device is a balloon.

Claim 6: The method of claim 1, wherein the drug is delivered at a flow rate of between about 0.1 and 10 cc/second.

Claim 9: A method for treating an intravascular occlusion, comprising:
delivering an occlusive device into a blood vessel to a site near said occlusion;

```
      ---  -----  -----------
?s au=(zadno? g? or zadno? , g?)
               0  AU=ZADNO? G?
               0  AU=ZADNO? , G?
      S1       0  AU=(ZADNO? G? OR ZADNO? , G?)
?show files
File 347:JAPIO Oct 1976-2003/May(Updated 030902)
         (c) 2003 JPO & JAPIO
File 348:EUROPEAN PATENTS 1978-2003/Sep W03
         (c) 2003 European Patent Office
File 349:PCT FULLTEXT 1979-2002/UB=20030925,UT=20030918
         (c) 2003 WIPO/Univentio
File 350:Derwent WPIX 1963-2003/UD,UM &UP=200361
         (c) 2003  Thomson Derwent
```

```
Set     Items   Description
S1      86453   (VENOUS OR VEIN? OR ARTERY OR ARTERI? OR VASCULAR? OR INTR-
             ?VASC? OR INTR?VEN? OR BLOOD?()VESSEL? OR VENAL OR CORONAR?)
S2      78348   OCCLUD? OR OCCLUSI? OR OBSTRUCT? OR STENOS? OR STENOT? OR -
             RESTENOS? OR RESTENOT? OR PLAQUE?
S3      39692   SCLERO? OR THROMB? OR BLOODCLOT? OR BLOOD()CLOT? OR ISCHEM-
             I? OR ARTER?SCLER? OR PLAQUING
S4        148   CALCIUM()DEPOSIT?
S5      67093   BALLOON? OR PLASTY? OR PLASTIE? ? OR ANGIOPLAST? OR OCCLU?-
             ()DEVICE? OR INFLAT? OR CARDIOPLAST?
S6          9   ARTERIOPLAST?
S7     874275   DELIVER? OR ADMINIST? OR INJECT? OR INFUS? OR PERFUS?
S8      39212   CATHETER? OR CANNULA? OR CANULA? OR TROCAR? OR LUMEN? OR H-
             OLLOW?(N)WIRE?
S9      85412   DRUG? OR NARCOTIC? OR OCCLU?(N)TREAT? OR ANTICOAGUL? OR AN-
             TI()COAGUL? OR THROMBYT?
S10      7240   RADIONUCLID? OR RADIO()NUCLID? OR RADIOISOTOP? OR RADIO()I-
             SOTOP? OR RADIOACTIVE()ISOTOP?
S11        57   RADIO()ACTIVE()ISOTOP?
S12    155305   FLOWRATE? OR FLOW()RATE? OR "CC" OR "C.C." OR CUBIC()CENTI-
             L?
S13     14340   S7(10N)(S9 OR S10 OR S11)
S14        34   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6) AND S8 AND S12
S15         6   S13 AND S14
?
?rd
>>>Duplicate detection is not supported for File 347.
>>>Duplicate detection is not supported for File 350.
>>>All specified files are unsupported, command ignored.
?show files
File 347:JAPIO Oct 1976-2003/May(Updated 030902)
         (c) 2003 JPO & JAPIO
File 350:Derwent WPIX 1963-2003/UD,UM &UP=200361
         (c) 2003  Thomson Derwent
?
```

15/5/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014901832 **Image available**
WPI Acc No: 2002-722538/200278
Related WPI Acc No: 1996-485524; 1997-202015; 1998-195201; 1999-359386
XRAM Acc No: C02-204401
XRPX Acc No: N02-569750

Expandable stent for implantation in patient, comprises open ended tubular metal body continuously coated on surface side wall structure with hydrophobic biostable elastomeric material and bio-active material

Patent Assignee: DING N (DING-I); HELMUS M (HELM-I)
Inventor: DING N; HELMUS M
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020091433	A1	20020711	US 95424884	A	19950419	200278 B
			US 95526273	A	19950911	
			US 96663490	A	19960613	
			US 96730542	A	19961011	
			US 9812443	A	19980123	
			US 9879645	A	19980515	
			US 200122607	A	20011217	

Priority Applications (No Type Date): US 200122607 A 20011217; US 95424884 A 19950419; US 95526273 A 19950911; US 96663490 A 19960613; US 96730542 A 19961011; US 9812443 A 19980123; US 9879645 A 19980515
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020091433	A1		22	A61F-002/06	CIP of application US 95424884 CIP of application US 95526273 Div ex application US 96663490 Cont of application US 96730542 CIP of application US 9812443 CIP of application US 9879645 Div ex patent US 5837313 CIP of patent US 6358556

Abstract (Basic): US 20020091433 A1

NOVELTY - An expandable stent for implantation in a patient, comprises an open ended tubular metal body (10) having a side wall structure. The structure is continuously coated with a coating containing a hydrophobic biostable elastomeric material and biologically active material, thereby conforms the structure in a manner that preserves the openings (18,20).

USE - For implantation in body **lumens** e.g. **vascular** implantation in urologic, pulmonary and gastrointestinal tracts.

ADVANTAGE - The expandable stent contains a coating of biostable elastomers incorporated with drug, thereby the drug is released controllably from the coating structure. The coating process enables the material to adherently conform to and cover the entire surface of the filaments of stent and preserving open lattice nature of the structure. The coatings on the stent releases the drugs over a period of time days to months to inhibit **thrombus** formation, smooth muscle cell migration and proliferation, inhibit hyperplasia and **restenosis** and encourage the formation of health neointimal tissue including endothelial cell regeneration and chronic patency after an **angioplasty** or stent placement. The expandable stent enables the long term **delivery** of **drugs** and minimizes interference with the independent mechanical or therapeutic benefits of the stent itself.

DESCRIPTION OF DRAWING(S) - The figure shows the stent section stretched or elongated for insertion.

Cylindrical tubular body (10)
Moving ends (18,20)
pp; 22 DwgNo 2A/15

Title Terms: EXPAND; STENT; IMPLANT; PATIENT; COMPRISE; OPEN; END; TUBE; METAL; BODY; CONTINUOUS; COATING; SURFACE; SIDE; WALL; STRUCTURE; HYDROPHOBIC; ELASTOMER; MATERIAL; BIO; ACTIVE; MATERIAL

Derwent Class: A96; B01; B04; B07; D22; P32
International Patent Class (Main): A61F-002/06
File Segment: CPI; EngPI

15/5/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014761599 **Image available**
WPI Acc No: 2002-582303/200262
Related WPI Acc No: 1998-018243; 1998-018245; 1998-018246; 1998-495477; 1998-495478; 1998-495560; 1998-495561; 1998-495562; 1999-357749; 1999-508737; 1999-518519; 2000-572309; 2000-664540; 2002-433264; 2003-089262; 2003-167050
XRAM Acc No: C02-164567
XRPX Acc No: N02-461716
Treatment of intravascular occlusion **comprises** delivering **fluid containing** occlusion - treating drug **such that at least portion of drug contacts with** intravascular occlusive device
Patent Assignee: ZADNO-AZIZI G (ZADN-I)
Inventor: ZADNO-AZIZI G
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020062119	A1	20020523	US 96650464	A	19960520	200262 B
			US 97812139	A	19970306	
			US 97812570	A	19970306	
			US 97812876	A	19970306	
			US 97813807	A	19970306	
			US 97813810	A	19970306	
			US 97933816	A	19970919	
			US 97975723	A	19971120	
			US 9849712	A	19980327	
			US 9849857	A	19980327	
			US 99270150	A	19990316	
			US 99314054	A	19990518	
			US 99415607	A	19991008	
			US 99438030	A	19991110	
			US 2000537471	A	20000324	
			US 2001837872	A	20010417	
			US 200135389	A	20011228	

Priority Applications (No Type Date): US 200135389 A 20011228; US 96650464 A 19960520; US 97812139 A 19970306; US 97812570 A 19970306; US 97812876 A 19970306; US 97813807 A 19970306; US 97813810 A 19970306; US 97933816 A 19970919; US 97975723 A 19971120; US 9849712 A 19980327; US 9849857 A 19980327; US 99270150 A 19990316; US 99314054 A 19990518; US 99415607 A 19991008; US 99438030 A 19991110; US 2000537471 A 20000324; US 2001837872 A 20010417
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020062119	A1		27	A61M-031/00	CIP of application US 96650464
					CIP of application US 97812139
					Cont of application US 97812570
					Cont of application US 97812876
					CIP of application US 97813807
					CIP of application US 97813810
					CIP of application US 97933816
					CIP of application US 97975723
					CIP of application US 9849712
					Cont of application US 9849857
					CIP of application US 99270150
					Cont of application US 99314054
					Cont of application US 99415607
					CIP of application US 99438030
					CIP of application US 2000537471
					CIP of application US 2001837872

Abstract (Basic): US 20020062119 A1

NOVELTY - Treatment of **intravascular occlusion** (18) comprises **delivering** fluid containing an **occlusion** - **treating drug** such that at least a portion of the drug contacts an **intravascular occlusive device** .

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a method for crossing an **intravascular occlusion** in a **blood vessel** comprising (i) delivering a **hollow wire** in a proximal to distal direction past the **occlusion** ; and (ii) delivering fluids through a **lumen** in the **hollow wire** to dissolve the **occlusion** while crossing of the **occlusion** with the **hollow wire** .

ACTIVITY - Cardiant; Circulatory-Gen.

No suitable biological data given.

MECHANISM OF ACTION - None given in source material.

USE - The method is used for treating an **intravascular occlusion** . It is also suited for treating **stenosis** or **occlusions** within saphenous **vein** grafts, **coronary arteries** , or cerebral **arteries** .

ADVANTAGE - The method decreases the risks to the patient.

DESCRIPTION OF DRAWING(S) - The figure is a partial cross-sectional view of a guidewire having an **occlusion balloon** and an aspiration **catheter** crossing an **occlusion** .

Guidewire (14)

Occlusion (18)

pp; 27 DwgNo 6A/13

Title Terms: TREAT; **INTRAVASCULAR** ; **OCCLUDE** ; COMPRISE; DELIVER; FLUID; CONTAIN; **OCCLUDE** ; TREAT; DRUG; PORTION; DRUG; CONTACT; **INTRAVASCULAR** ; **OCCLUDE** ; DEVICE

Derwent Class: B07; P34

International Patent Class (Main): A61M-031/00

File Segment: CPI; EngPI

15/5/3 (Item 3 from file: 350)

DIALOG(R)File 350:Derwent WPIX

014270981 **Image available**

WPI Acc No: 2002-091682/200213

Related WPI Acc No: 2001-362957

XRAM Acc No: C02-028503

XRPX Acc No: N02-067529

Occlusion catheter **for ascending aorta comprises** catheter **tube having first and second** lumens **and drug release aperture, and** balloon

Patent Assignee: VAYU KK (VAYU-N); KUMENO T (KUME-I); TSUTSUI N (TSUT-I); YOZU R (YOZU-I)

Inventor: KUMENO T; TSUTSUI N; YOZU R

Number of Countries: 029 Number of Patents: 004

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 1159984	A1	20011205	EP 2001108396	A	20010403	200213	B
CA 2342597	A1	20011129	CA 2342597	A	20010403	200213	
JP 2002052083	A	20020219	JP 2001104525	A	20010403	200229	
US 20030167038	A1	20030904	US 2001846002	A	20010430	200359	

Priority Applications (No Type Date): JP 2000158152 A 20000529; JP 99283371 A 19991004

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 1159984	A1	E	27	A61M-025/10	
	Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR				
CA 2342597	A1	E		A61M-025/04	
JP 2002052083	A		11	A61M-025/00	
US 20030167038	A1			A61M-029/00	

Abstract (Basic): EP 1159984 A1

NOVELTY - An **occlusion catheter** comprises a **catheter** tube having a first **lumen** (s) and a second **lumen** , and a **balloon** provided on the outer circumference of the distal end of the tube. The tube is provided with a drug release aperture for releasing a drug supplied through the second **lumen** .

DETAILED DESCRIPTION - An **occlusion catheter** comprises a **catheter** tube (3) having a first **lumen** (s) and a second **lumen** , and a **balloon** (5) provided on the outer circumference of the distal end of the tube which **inflates** /deflates with supply or drainage of a fluid through the first **lumen** to **obstruct** the blood flow within the ascending aorta when **inflated** . The tube is provided with a drug release aperture (23) for releasing a drug supplied through the second **lumen** in the position closer to the proximal end than the site where the blood flow is **obstructed** by the **balloon** on the outer circumference of the distal end of the tube.

An INDEPENDENT CLAIM is also included for a method of using an **occlusion catheter** comprising making an incision or a hole in the chest to provide access to the ascending aorta (1) from the outside, creating an opening at an insertion site of the aorta, expanding the opening with a dilator, inserting the **occlusion catheter** into the aorta through the opening, fixing the **catheter** to the aorta, placing a **balloon** in a proper indwelling position, **inflating** the **balloon** to **occlude** the aorta, and releasing a cardiac muscle protective **drug** from a **drug** release aperture to **deliver** the **drug** to the vicinity of the **coronary** ostium.

USE - For the ascending aorta.

ADVANTAGE - The device is capable of **obstructing** blood flow within the ascending aorta without inserting through the femoral **artery** . It enables **delivery** of a cardiac muscle protective **drug** to the vicinity of the **coronary** ostium, and is capable of maintaining the condition where the **balloon** is placed in proper indwelling position. It also facilitates increase of the **flow rate** of the cardiac muscle protective drug.

DESCRIPTION OF DRAWING(S) - The figure shows a side view of the **occlusion catheter** .

Ascending aorta (1)
Catheter tube (3)
Balloon (5)
Guide wire (22)
Drug release aperture (23)
pp; 27 DwgNo 1/15

Title Terms: **OCCLUDE** ; **CATHETER** ; ASCEND; AORTA; COMPRISE; **CATHETER** ; TUBE; FIRST; SECOND; **LUMEN** ; DRUG; RELEASE; APERTURE; **BALLOON**
Derwent Class: A96; B07; P31; P34
International Patent Class (Main): A61M-025/00; A61M-025/04; A61M-025/10; A61M-029/00
International Patent Class (Additional): A61B-017/12; A61M-001/36; A61M-039/00
File Segment: CPI; EngPI

15/5/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013750721 **Image available**
WPI Acc No: 2001-234950/200124
XRAM Acc No: C01-070347
XRPX Acc No: N01-168024

Pressure-based lumen **mapping apparatus for e.g.,** stenosis **identification by set of pressure measurements, comprises pressure wire, pressure sensor, pull back mechanism, and processor**

Patent Assignee: FLORENCE MEDICAL LTD (FLOR-N)
Inventor: BARAK C; DGANY E; NOSKOWICZ S H; SHALMAN E
Number of Countries: 094 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200113779	A2	20010301	WO 2000IL508	A	20000824	200124	B

AU 200067222 A 20010319 AU 200067222 A 20000824 200136

Priority Applications (No Type Date): US 99155110 P 19990922; US 99150567 P 19990825

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200113779	A2	E	78	A61B-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200067222 A A61B-000/00 Based on patent WO 200113779

Abstract (Basic): WO 200113779 A2

NOVELTY - A pressure-based **lumen** mapping apparatus includes:

(i) a pressure wire for insertion to the **lumen** ;

(ii) a pressure sensor connected to the pressure wire for measuring pressure inside the **lumen** ;

(iii) a pull back mechanism for moving the pressure wire in predetermined manner; and

(iv) a processor for processing the pressure measurements

DETAILED DESCRIPTION - A pressure-based **lumen** mapping apparatus comprises:

(i) a pressure wire (60) for insertion to the **lumen** ;

(ii) a pressure sensor (40) connected to the pressure wire for measuring pressure inside the **lumen** ;

(iii) a pull back mechanism (50) for moving the pressure wire in predetermined manner; and

(iv) a processor for processing the pressure measurements to obtain parameters of fluid dynamics equation.

The pressure is measured at various points during the movement of the pressure wire.

The processor uses the pressure measurement to inversely obtain parameters of a fluid dynamics equation for mapping the **lumen** .

An INDEPENDENT CLAIM is also included for a method of pressure-based **lumen** mapping by:

(a) inserting a pressure wire with pressure sensor to the **lumen** ;

(b) moving the pressure wire from one point to another point along the **lumen** , while simultaneously measuring the pressure; and

(c) using the pressure measurement obtained during the movement, obtaining parameters of a fluid dynamics equation to provide at least one parameter of the **lumen** .

USE - The apparatus is used for:

(1) **stenosis** identification by set of pressure measurements;

(2) **stenosis** localization in the **artery** ;

(3) determining length, minimal diameter, and severity of **stenosis** ;

(4) hemodynamic reconstruction of **stenosis** geometry;

(5) calculating average **flow rate** in the **occluded artery** ;

(6) determination of average blood velocity; and

(7) determination of pulsatile index from the known flow in the **artery** .

The above data are essential for optimal selection of stent or **balloon** for the required **inflated** pressure and contact area, and for **drug delivery** .

DESCRIPTION OF DRAWING(S) - The figure is a schematic isometric view of the pressure-based **lumen** mapping apparatus.

Pressure sensor (40)

Pull back mechanism (50)

Pressure wire (60)

pp; 78 DwgNo 1/33

Title Terms: PRESSURE; BASED; **LUMEN** ; MAP; APPARATUS; **STENOSIS** ; IDENTIFY ; SET; PRESSURE; MEASURE; COMPRISE; PRESSURE; WIRE; PRESSURE; SENSE; PULL ; BACK; MECHANISM; PROCESSOR

Derwent Class: B07; P31

International Patent Class (Main): A61B-000/00

File Segment: CPI; EngPI

15/5/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012793966
WPI Acc No: 1999-600195/199951
Related WPI Acc No: 1999-518523
XRAM Acc No: C99-174650
XRPX Acc No: N99-442375
Inhibition of restenosis **by local application of e.g. hydrogen peroxide, thus avoiding use of radiation therapy**
Patent Assignee: SCIMED LIFE SYSTEMS INC (SCIM-N)
Inventor: HASTINGS R N; UNGS M T; URICK M J; WANG L; YANG D
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5951458	A	19990914	US 96608655	A	19960229	199951	B
			US 97782471	A	19970110		
			US 97812248	A	19970306		
			US 97868482	A	19970603		
			US 97905296	A	19970801		

Priority Applications (No Type Date): US 97905296 A 19970801; US 96608655 A 19960229; US 97782471 A 19970110; US 97812248 A 19970306; US 97868482 A 19970603
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5951458	A		24	A61M-005/00	CIP of application US 96608655
					CIP of application US 97782471
					CIP of application US 97812248
					CIP of application US 97868482
					CIP of patent US 5855546
					CIP of patent US 5882290

Abstract (Basic): US 5951458 A
NOVELTY - **Restenosis** of **blood vessels** is inhibited by local application of an oxidizing agent, hydroxyl ions or a free radical generating agent.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(A) inhibiting **restenosis** of a **blood vessel** wall, comprising locally applying an oxidizing agent to the vessel walls;
(B) inhibiting **restenosis** of a **blood vessel** wall, comprising locally applying a free radical generating agent to the vessel walls; and
(C) inhibiting **restenosis** of a **stenosed coronary** vessel region, comprising locally applying hydroxyl ions to the vessel region.
ACTIVITY - Vasotropic; antirestenosis.
MECHANISM OF ACTION - None given.
USE - The processes are useful for preventing **restenosis** of **blood vessels**, especially **coronary arteries**.
ADVANTAGE - Local delivery of oxidizing agent avoids the need for the specialized equipment and personnel associated with use of radiation to prevent **restenosis**.
pp; 24 DwgNo 0/23
Title Terms: INHIBIT; LOCAL; APPLY; HYDROGEN; PEROXIDE; AVOID; RADIATE; THERAPEUTIC
Derwent Class: B06; B07; P34
International Patent Class (Main): A61M-005/00
File Segment: CPI; EngPI

15/5/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

010742331 **Image available**
WPI Acc No: 1996-239286/199624
XRAM Acc No: C96-076341
XRPX Acc No: N96-200305

Device for infusing agent adjacent to blood vessel **wall - has ports in distal segment which can be formed into expanded helical coil to leave high** flow rate **central** lumen

Patent Assignee: MICRO THERAPEUTICS INC (MICR-N)
Inventor: CRAGG A H; EVANS S M; WALLACE G B; CRAGG M D A H
Number of Countries: 019 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9613295	A1	19960509	WO 95US13414	A	19951018	199624	B
CA 2160847	A	19960421	CA 2160847	A	19951018	199634	
US 5554114	A	19960910	US 94326609	A	19941020	199642	
EP 787018	A1	19970806	EP 95938787	A	19951018	199736	
			WO 95US13414	A	19951018		
JP 10509350	W	19980914	WO 95US13414	A	19951018	199847	
			JP 96514640	A	19951018		

Priority Applications (No Type Date): US 94326609 A 19941020
Cited Patents: US 5116309
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9613295	A1	E	31	A61M-025/00	
Designated States (National): JP					
Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
US 5554114	A		13	A61M-025/00	
EP 787018	A1	E		A61M-025/00	Based on patent WO 9613295
Designated States (Regional): BE DE FR GB IT NL					
JP 10509350	W		35	A61M-025/00	Based on patent WO 9613295
CA 2160847	A			A61M-025/01	

Abstract (Basic): WO 9613295 A

Device for **infusing** a **drug** or other agent into a peripheral low blood **flow rate** region adjacent to a **blood vessel** wall comprises a tube with infusion ports (18) along and around a distal segment (26) following a proximal straight segment. The distal segment can be formed into an expanded helical coil of not less than 2 turns leaving a central higher **flow rate lumen** . In the coil, the ports face the vessel wall, adjacent coil turns and the central **lumen** . The distal segment pref. has a sheath around a coiled wire and is biased towards expanded state so that it can be contracted by a core wire for advancement and expand when the wire is withdrawn.

USE - E.g. to deliver a lytic agent to a **blood clot** , or an agent to a vessel wall after **angioplasty** .

ADVANTAGE - Permits simpler and less expensive **drug delivery** to a vessel wall or **obstruction** while allowing the blood to flow centrally.

Dwg.1/13

Title Terms: DEVICE; INFUSION; AGENT; ADJACENT; BLOOD; VESSEL; WALL; PORT; DISTAL; SEGMENT; CAN; FORMING; EXPAND; HELICAL; COIL; LEAVE; HIGH; FLOW; RATE; CENTRAL; **LUMEN**
Derwent Class: B07; P34
International Patent Class (Main): A61M-025/00; A61M-025/01
International Patent Class (Additional): A61M-025/09
File Segment: CPI; EngPI

22/5,K/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014901832 **Image available**
WPI Acc No: 2002-722538/200278
Related WPI Acc No: 1996-485524; 1997-202015; 1998-195201; 1999-359386
XRAM Acc No: C02-204401
XRPX Acc No: N02-569750

Expandable stent for implantation in patient, comprises open ended tubular metal body continuously coated on surface side wall structure with hydrophobic biostable elastomeric material and bio-active material

Patent Assignee: DING N (DING-I); HELMUS M (HELM-I)
Inventor: DING N; HELMUS M

Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020091433	A1	20020711	US 95424884	A	19950419	200278 B
			US 95526273	A	19950911	
			US 96663490	A	19960613	
			US 96730542	A	19961011	
			US 9812443	A	19980123	
			US 9879645	A	19980515	
			US 200122607	A	20011217	

Priority Applications (No Type Date): US 200122607 A 20011217; US 95424884 A 19950419; US 95526273 A 19950911; US 96663490 A 19960613; US 96730542 A 19961011; US 9812443 A 19980123; US 9879645 A 19980515
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020091433	A1		22	A61F-002/06	CIP of application US 95424884 CIP of application US 95526273 Div ex application US 96663490 Cont of application US 96730542 CIP of application US 9812443 CIP of application US 9879645 Div ex patent US 5837313 CIP of patent US 6358556

Abstract (Basic): US 20020091433 A1

NOVELTY - An expandable stent for implantation in a patient, comprises an open ended tubular metal body (10) having a side wall structure. The structure is continuously coated with a coating containing a hydrophobic biostable elastomeric material and biologically active material, thereby conforms the structure in a manner that preserves the openings (18,20).

USE - For implantation in body **lumens** e.g. **vascular** implantation in urologic, pulmonary and gastrointestinal tracts.

ADVANTAGE - The expandable stent contains a coating of biostable elastomers incorporated with drug, thereby the drug is released controllably from the coating structure. The coating process enables the material to adherently conform to and cover the entire surface of the filaments of stent and preserving open lattice nature of the structure. The coatings on the stent releases the drugs over a period of time days to months to inhibit **thrombus** formation, smooth muscle cell migration and proliferation, inhibit hyperplasia and **restenosis** and encourage the formation of health neointimal tissue including endothelial cell regeneration and chronic patency after an **angioplasty** or stent placement. The expandable stent enables the long term **delivery** of **drugs** and minimizes interference with the independent mechanical or therapeutic benefits of the stent itself.

DESCRIPTION OF DRAWING(S) - The figure shows the stent section stretched or elongated for insertion.

Cylindrical tubular body (10)
Moving ends (18,20)
pp; 22 DwgNo 2A/15

Title Terms: EXPAND; STENT; IMPLANT; PATIENT; COMPRISE; OPEN; END; TUBE; METAL; BODY; CONTINUOUS; COATING; SURFACE; SIDE; WALL; STRUCTURE; HYDROPHOBIC; ELASTOMER; MATERIAL; BIO; ACTIVE; MATERIAL

Derwent Class: A96; B01; B04; B07; D22; P32
International Patent Class (Main): A61F-002/06
File Segment: CPI; EngPI

Abstract (Basic):
... For implantation in body **lumens** e.g. **vascular** implantation in urologic, pulmonary and gastrointestinal tracts...

...the stent releases the drugs over a period of time days to months to inhibit **thrombus** formation, smooth muscle cell migration and proliferation, inhibit hyperplasia and **restenosis** and encourage the formation of health neointimal tissue including endothelial cell regeneration and chronic patency after an **angioplasty** or stent placement. The expandable stent enables the long term **delivery** of **drugs** and minimizes interference with the independent mechanical or therapeutic benefits of the stent itself...

Technology Focus:
... an air brush at a pressure of 15-25 psi, and at a spray nozzle **flow rate** of 4-10 ml. The coating comprises one or more coating layers...

22/5,K/2 (Item 2 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014761599 **Image available**
WPI Acc No: 2002-582303/200262
Related WPI Acc No: 1998-018243; 1998-018245; 1998-018246; 1998-495477; 1998-495478; 1998-495560; 1998-495561; 1998-495562; 1999-357749; 1999-508737; 1999-518519; 2000-572309; 2000-664540; 2002-433264; 2003-089262; 2003-167050
XRAM Acc No: C02-164567
XRPX Acc No: N02-461716
Treatment of intravascular occlusion **comprises** delivering **fluid containing** occlusion - treating drug **such that at least portion of drug contacts with** intravascular occlusive device
Patent Assignee: ZADNO-AZIZI G (ZADN-I)
Inventor: ZADNO-AZIZI G
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20020062119	A1	20020523	US 96650464	A	19960520	200262 B
			US 97812139	A	19970306	
			US 97812570	A	19970306	
			US 97812876	A	19970306	
			US 97813807	A	19970306	
			US 97813810	A	19970306	
			US 97933816	A	19970919	
			US 97975723	A	19971120	
			US 9849712	A	19980327	
			US 9849857	A	19980327	
			US 99270150	A	19990316	
			US 99314054	A	19990518	
			US 99415607	A	19991008	
			US 99438030	A	19991110	
			US 2000537471	A	20000324	
			US 2001837872	A	20010417	
			US 200135389	A	20011228	

Priority Applications (No Type Date): US 200135389 A 20011228; US 96650464 A 19960520; US 97812139 A 19970306; US 97812570 A 19970306; US 97812876 A 19970306; US 97813807 A 19970306; US 97813810 A 19970306; US 97933816 A 19970919; US 97975723 A 19971120; US 9849712 A 19980327; US 9849857 A 19980327; US 99270150 A 19990316; US 99314054 A 19990518; US 99415607 A 19991008; US 99438030 A 19991110; US 2000537471 A 20000324; US 2001837872 A 20010417
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20020062119 A1			27	A61M-031/00	CIP of application US 96650464 CIP of application US 97812139 Cont of application US 97812570 Cont of application US 97812876 CIP of application US 97813807 CIP of application US 97813810 CIP of application US 97933816 CIP of application US 97975723 CIP of application US 9849712 Cont of application US 9849857 CIP of application US 99270150 Cont of application US 99314054 Cont of application US 99415607 CIP of application US 99438030 CIP of application US 2000537471 CIP of application US 2001837872

Abstract (Basic): US 20020062119 A1

NOVELTY - Treatment of **intravascular occlusion** (18) comprises **delivering** fluid containing an **occlusion - treating drug** such that at least a portion of the drug contacts an **intravascular occlusive device** .

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a method for crossing an **intravascular occlusion** in a **blood vessel** comprising (i) delivering a **hollow wire** in a proximal to distal direction past the **occlusion** ; and (ii) delivering fluids through a **lumen** in the **hollow wire** to dissolve the **occlusion** while crossing of the **occlusion** with the **hollow wire** .

ACTIVITY - Cardiant; Circulatory-Gen.

No suitable biological data given.

MECHANISM OF ACTION - None given in source material.

USE - The method is used for treating an **intravascular occlusion** . It is also suited for treating **stenosis** or **occlusions** within saphenous **vein** grafts, **coronary arteries** , or cerebral **arteries** .

ADVANTAGE - The method decreases the risks to the patient.

DESCRIPTION OF DRAWING(S) - The figure is a partial cross-sectional view of a guidewire having an **occlusion balloon** and an aspiration **catheter** crossing an **occlusion** .

Guidewire (14)

Occlusion (18)

pp; 27 DwgNo 6A/13

Title Terms: TREAT; **INTRAVASCULAR** ; **OCCLUDE** ; COMPRISE; DELIVER; FLUID; CONTAIN; **OCCLUDE** ; TREAT; DRUG; PORTION; DRUG; CONTACT; **INTRAVASCULAR** ; **OCCLUDE** ; DEVICE

Derwent Class: B07; P34

International Patent Class (Main): A61M-031/00

File Segment: CPI; EngPI

Treatment of intravascular occlusion **comprises** delivering **fluid containing** occlusion - treating drug **such that at least portion of drug contacts with** intravascular occlusive device

Abstract (Basic):

... Treatment of **intravascular occlusion** (18) comprises **delivering** fluid containing an **occlusion - treating drug** such that at least a portion of the drug contacts an **intravascular occlusive device** .

... An INDEPENDENT CLAIM is included for a method for crossing an **intravascular occlusion** in a **blood vessel** comprising (i) delivering a **hollow wire** in a proximal to distal direction past the **occlusion** ; and (ii) delivering fluids through a **lumen** in the **hollow wire** to dissolve the **occlusion** while crossing of the **occlusion** with the **hollow wire** .

...

...The method is used for treating an **intravascular occlusion** . It is also suited for treating **stenosis** or **occlusions** within saphenous

22/5,K/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014270981 **Image available**
WPI Acc No: 2002-091682/200213
Related WPI Acc No: 2001-362957
XRAM Acc No: C02-028503
XRPX Acc No: N02-067529
Occlusion catheter **for ascending aorta comprises** catheter **tube having first and second** lumens **and drug release aperture, and** balloon
Patent Assignee: VAYU KK (VAYU-N); KUMENO T (KUME-I); TSUTSUI N (TSUT-I); YOZU R (YOZU-I)
Inventor: KUMENO T; TSUTSUI N; YOZU R
Number of Countries: 029 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 1159984	A1	20011205	EP 2001108396	A	20010403	200213	B
CA 2342597	A1	20011129	CA 2342597	A	20010403	200213	
JP 2002052083	A	20020219	JP 2001104525	A	20010403	200229	
US 20030167038	A1	20030904	US 2001846002	A	20010430	200359	

Priority Applications (No Type Date): JP 2000158152 A 20000529; JP 99283371 A 19991004
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 1159984	A1	E	27	A61M-025/10	
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
CA 2342597	A1	E		A61M-025/04	
JP 2002052083	A		11	A61M-025/00	
US 20030167038	A1			A61M-029/00	

Abstract (Basic): EP 1159984 A1

NOVELTY - An **occlusion catheter** comprises a **catheter** tube having a first **lumen** (s) and a second **lumen** , and a **balloon** provided on the outer circumference of the distal end of the tube. The tube is provided with a drug release aperture for releasing a drug supplied through the second **lumen** .

DETAILED DESCRIPTION - An **occlusion catheter** comprises a **catheter** tube (3) having a first **lumen** (s) and a second **lumen** , and a **balloon** (5) provided on the outer circumference of the distal end of the tube which **inflates** /deflates with supply or drainage of a fluid through the first **lumen** to **obstruct** the blood flow within the ascending aorta when **inflated** . The tube is provided with a drug release aperture (23) for releasing a drug supplied through the second **lumen** in the position closer to the proximal end than the site where the blood flow is **obstructed** by the **balloon** on the outer circumference of the distal end of the tube.

An INDEPENDENT CLAIM is also included for a method of using an **occlusion catheter** comprising making an incision or a hole in the chest to provide access to the ascending aorta (1) from the outside, creating an opening at an insertion site of the aorta, expanding the opening with a dilator, inserting the **occlusion catheter** into the aorta through the opening, fixing the **catheter** to the aorta, placing a **balloon** in a proper indwelling position, **inflating** the **balloon** to **occlude** the aorta, and releasing a cardiac muscle protective **drug** from a **drug** release aperture to **deliver** the **drug** to the vicinity of the **coronary** ostium.

USE - For the ascending aorta.

ADVANTAGE - The device is capable of **obstructing** blood flow within the ascending aorta without inserting through the femoral **artery** . It enables **delivery** of a cardiac muscle protective **drug** to the vicinity of the **coronary** ostium, and is capable of maintaining the condition where the **balloon** is placed in proper indwelling position. It also facilitates increase of the **flow rate** of the cardiac muscle protective drug.

DESCRIPTION OF DRAWING(S) - The figure shows a side view of the

22/5,K/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014270981 **Image available**
WPI Acc No: 2002-091682/200213
Related WPI Acc No: 2001-362957
XRAM Acc No: C02-028503
XRPX Acc No: N02-067529
Occlusion catheter **for ascending aorta comprises** catheter **tube having first and second** lumens **and drug release aperture, and** balloon
Patent Assignee: VAYU KK (VAYU-N); KUMENO T (KUME-I); TSUTSUI N (TSUT-I); YOZU R (YOZU-I)
Inventor: KUMENO T; TSUTSUI N; YOZU R
Number of Countries: 029 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 1159984	A1	20011205	EP 2001108396	A	20010403	200213	B
CA 2342597	A1	20011129	CA 2342597	A	20010403	200213	
JP 2002052083	A	20020219	JP 2001104525	A	20010403	200229	
US 20030167038	A1	20030904	US 2001846002	A	20010430	200359	

Priority Applications (No Type Date): JP 2000158152 A 20000529; JP 99283371 A 19991004
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 1159984	A1	E	27	A61M-025/10	
Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
CA 2342597	A1	E		A61M-025/04	
JP 2002052083	A		11	A61M-025/00	
US 20030167038	A1			A61M-029/00	

Abstract (Basic): EP 1159984 A1

NOVELTY - An **occlusion catheter** comprises a **catheter** tube having a first **lumen** (s) and a second **lumen** , and a **balloon** provided on the outer circumference of the distal end of the tube. The tube is provided with a drug release aperture for releasing a drug supplied through the second **lumen** .

DETAILED DESCRIPTION - An **occlusion catheter** comprises a **catheter** tube (3) having a first **lumen** (s) and a second **lumen** , and a **balloon** (5) provided on the outer circumference of the distal end of the tube which **inflates** /deflates with supply or drainage of a fluid through the first **lumen** to **obstruct** the blood flow within the ascending aorta when **inflated** . The tube is provided with a drug release aperture (23) for releasing a drug supplied through the second **lumen** in the position closer to the proximal end than the site where the blood flow is **obstructed** by the **balloon** on the outer circumference of the distal end of the tube.

An INDEPENDENT CLAIM is also included for a method of using an **occlusion catheter** comprising making an incision or a hole in the chest to provide access to the ascending aorta (1) from the outside, creating an opening at an insertion site of the aorta, expanding the opening with a dilator, inserting the **occlusion catheter** into the aorta through the opening, fixing the **catheter** to the aorta, placing a **balloon** in a proper indwelling position, **inflating** the **balloon** to **occlude** the aorta, and releasing a cardiac muscle protective **drug** from a **drug** release aperture to **deliver** the **drug** to the vicinity of the **coronary** ostium.

USE - For the ascending aorta.

ADVANTAGE - The device is capable of **obstructing** blood flow within the ascending aorta without inserting through the femoral **artery** . It enables **delivery** of a cardiac muscle protective **drug** to the vicinity of the **coronary** ostium, and is capable of maintaining the condition where the **balloon** is placed in proper indwelling position. It also facilitates increase of the **flow rate** of the cardiac muscle protective drug.

DESCRIPTION OF DRAWING(S) - The figure shows a side view of the

occlusion catheter .
Ascending aorta (1)
Catheter tube (3)
Balloon (5)
Guide wire (22)
Drug release aperture (23)
pp; 27 DwgNo 1/15
Title Terms: **OCCLUDE** ; **CATHETER** ; ASCEND; AORTA; COMPRISE; **CATHETER** ; TUBE; FIRST; SECOND; **LUMEN** ; DRUG; RELEASE; APERTURE; **BALLOON**
Derwent Class: A96; B07; P31; P34
International Patent Class (Main): A61M-025/00; A61M-025/04; A61M-025/10; A61M-029/00
International Patent Class (Additional): A61B-017/12; A61M-001/36; A61M-039/00
File Segment: CPI; EngPI

Occlusion catheter **for ascending aorta comprises** catheter **tube having first and second** lumens **and drug release aperture, and** balloon

Abstract (Basic):
... An **occlusion catheter** comprises a **catheter** tube having a first **lumen** (s) and a second **lumen** , and a **balloon** provided on the outer circumference of the distal end of the tube. The tube is provided with a drug release aperture for releasing a drug supplied through the second **lumen** .
... An **occlusion catheter** comprises a **catheter** tube (3) having a first **lumen** (s) and a second **lumen** , and a **balloon** (5) provided on the outer circumference of the distal end of the tube which **inflates** /deflates with supply or drainage of a fluid through the first **lumen** to **obstruct** the blood flow within the ascending aorta when **inflated** . The tube is provided with a drug release aperture (23) for releasing a drug supplied through the second **lumen** in the position closer to the proximal end than the site where the blood flow is **obstructed** by the **balloon** on the outer circumference of the distal end of the tube...

...An INDEPENDENT CLAIM is also included for a method of using an **occlusion catheter** comprising making an incision or a hole in the chest to provide access to the...

...at an insertion site of the aorta, expanding the opening with a dilator, inserting the **occlusion catheter** into the aorta through the opening, fixing the **catheter** to the aorta, placing a **balloon** in a proper indwelling position, **inflating** the **balloon** to **occlude** the aorta, and releasing a cardiac muscle protective **drug** from a **drug** release aperture to **deliver** the **drug** to the vicinity of the **coronary** ostium...

...The device is capable of **obstructing** blood flow within the ascending aorta without inserting through the femoral **artery** . It enables **delivery** of a cardiac muscle protective **drug** to the vicinity of the **coronary** ostium, and is capable of maintaining the condition where the **balloon** is placed in proper indwelling position. It also facilitates increase of the **flow rate** of the cardiac muscle protective drug...

...The figure shows a side view of the **occlusion catheter** .
...

... **Catheter** tube (3...

... **Balloon** (5
Technology Focus:
... Preferred Device: At least two drug release apertures are formed proximally than the **balloon** in different directions, respectively, relative to the axial direction of the tube. The **catheter** tube includes a portion from the distal end to a point reinforced with a reinforcement mechanism. The concavity is formed at each end of the **balloon** . The device further comprises a valve provided within the

second **lumen** having a structure capable of passing a guide wire (22) and shutting the fluid flow...

...Preferred Component: The **balloon** is made of polyurethane.
Title Terms: **OCCLUDE** ;

22/5,K/4 (Item 4 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2003 Thomson Derwent. All rts. reserv.

013797292 **Image available**
WPI Acc No: 2001-281504/200129
Related WPI Acc No: 2001-367781
XRAM Acc No: C01-085527
XRPX Acc No: N01-200751
Mechanical pump for use in a medical device, for removing unwanted tissues from body lumens **or** blood vessels **, comprises an inner tube, coiled rotor element disposed over outer surface of tube and a jacket securing the rotor to the tube**
Patent Assignee: BACCHUS VASCULAR INC (BACC-N)
Inventor: DEMARAIS D M; EVANS M A; EVERSULL C S; LEEFLANG S A; TANNER J C; WATANABE G A; DEMARAIS D
Number of Countries: 023 Number of Patents: 004
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200119444	A1	20010322	WO 2000US25581	A	20000918	200129	B
AU 200077038	A	20010417	AU 200077038	A	20000918	200140	
EP 1225949	A1	20020731	EP 2000966741	A	20000918	200257	
			WO 2000US25581	A	20000918		
US 20020151906	A1	20021017	US 99454517	A	19991206	200270	
			US 2002162276	A	20020603		

Priority Applications (No Type Date): US 2000590915 A 20000609; US 99154752 P 19990917; US 99454517 A 19991206; US 2002162276 A 20020603
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200119444	A1	E	49	A61M-029/00	
Designated States (National): AU CA JP					
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
AU 200077038	A			A61M-029/00	Based on patent WO 200119444
EP 1225949	A1	E		A61M-029/00	Based on patent WO 200119444
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 20020151906	A1			A61B-017/22	Cont of application US 99454517

Abstract (Basic): WO 200119444 A1

NOVELTY - A mechanical pump for use in a medical device comprises an elongated hollow, flexible inner tube (122) with a proximal end, a distal end (132) and a central **lumen** , a first coiled rotor element (142) (with a distal end and a proximal end) disposed over an outer surface of the inner tube and a jacket which secures the coil rotor element to the outer surface of the inner tube.

DETAILED DESCRIPTION - A mechanical pump for use in a medical device comprises an elongated hollow, flexible inner tube (122) with a proximal end, a distal end (132) and a central **lumen** , a first coiled rotor element (142) (with a distal end and a proximal end) disposed over an outer surface of the inner tube and a jacket which secures the coil rotor element to the outer surface of the inner tube.

INDEPENDENT CLAIMS are also included for the following:

(1) an over-the-wire material transport **catheter** comprising a **catheter** body (112) having a proximal end, a distal end and a **lumen** (130) between these and an impeller which is rotatable within the **lumen** of the **catheter** body. The impeller comprises a tubular shaft having a central guidewire **lumen** and a helical rotor (148) extending at least partially over an exterior surface;

(2) a selective infusion-aspiration **catheter** comprising a

catheter body having a proximal end, a distal end and a **lumen** between these, an impeller rotatable within the **lumen** of the **catheter** body and a driver coupled to the impeller to selectively rotate the impeller in a first direction to induce aspiration through the **catheter** body **lumen** or in a second direction to induce infusion through the **catheter** body;

(3) a circulation **catheter** comprising a **catheter** body having a proximal end, a distal end and a **lumen** between these and a first impeller arranged in a **lumen** of the **catheter** body to aspirate materials from the distal end to the proximal end of the **catheter** body and a second impeller arranged in a **lumen** of the **catheter** body to infuse materials from the proximal end to the distal end of the **catheter** body;

(4) a method for making a mechanical pump for use in a medical device comprising:

(a) placing a resilient coiled rotor over an outer surface of a hollow flexible tube; and

(b) forming a jacket over at least a portion of the outer surface of the tube and the coiled rotor so that the coiled rotor is secured to the outer surface of the flexible tube;

(5) a method for making a mechanical pump for use in a medical device comprising forming a helical channel in an outer surface of a hollow flexible tube;

(6) a method for transporting materials between a target site in a body **lumen** of a patient and a location external to the patient comprising:

(a) introducing a distal end of a **catheter** to the target site over a guidewire and rotating; and

(b) rotating a first impeller over a guidewire within a **lumen** of the **catheter** to transport material between the distal and proximal end of the **catheter** ; and

(7) a kit comprising a **catheter** and instructions for its use.

USE - For use in/as medical devices such as **catheters** (claimed) for removing unwanted tissues such as **thrombus** , atheroma, fluids, polyps, cysts or other **obstructive** matter from body **lumens** such as **blood vessels** , ureters, bile ducts or fallopian tubes. The material transport **catheters** may be used to **infuse thrombolytic** and other therapeutic agents and/or aspirate fragmented clot, **thrombus** and other **occlusive** materials in conjunction with **angioplasty** , atherectomy, laser ablation, embolectomy, endarterectomy and other **intravascular** interventions.

ADVANTAGE - The **catheter** efficiently evacuates the fragmented material from the **blood vessel** or body **lumen** , with continuous fluid infusion. Larger particles of fragmented material can be aspirated within a short time. Use of two rotors provides for higher volumetric and mass flows than is achievable using one rotor and the coiled rotors allow for the provision of different fluid **flow rates** to different portions of the **catheter** . The impeller and rotor provide two different streams of the same or different materials to a single or multiple locations within the **catheter** . Two different fluids (chemicals and reagent that cannot be premixed prior to delivery) can also be mixed in situ at the distal end of the **catheter** . Use of a single impeller with a bi-directional flow allows circulation and recirculation of material to a target side within a patient body **lumen** to be achieved.

DESCRIPTION OF DRAWING(S) - The figure shows the partially broken, detailed view of distal end of the clot disruption **catheter** and mechanical pump.

Catheter body (112)
Flexible inner tube (122)
Expansible cage (126)
Lumen (130)
Distal end of shaft (132)
Macerator (140)
Coiled rotor element (142)
Helical rotor (148)

pp; 49 DwgNo 5A/9

Title Terms: MECHANICAL; PUMP; MEDICAL; DEVICE; REMOVE; UNWANTED; TISSUE;

BODY; **LUMEN** ; BLOOD; VESSEL; COMPRISE; INNER; TUBE; COIL; ROTOR; ELEMENT ; DISPOSABLE; OUTER; SURFACE; TUBE; JACKET; SECURE; ROTOR; TUBE
Derwent Class: B07; P31; P34
International Patent Class (Main): A61B-017/22; A61M-029/00
File Segment: CPI; EngPI

Mechanical pump for use in a medical device, for removing unwanted tissues from body lumens **or** blood vessels , **comprises an inner tube, coiled rotor element disposed over outer surface of tube and a...**

Abstract (Basic):

... flexible inner tube (122) with a proximal end, a distal end (132) and a central **lumen** , a first coiled rotor element (142) (with a distal end and a proximal end) disposed...

... flexible inner tube (122) with a proximal end, a distal end (132) and a central **lumen** , a first coiled rotor element (142) (with a distal end and a proximal end) disposed...

...1) an over-the-wire material transport **catheter** *comprising a* **catheter** body (112) having a proximal end, a distal end and a **lumen** *(130)* between these and an impeller which is rotatable within the **lumen** of the **catheter** body. The impeller comprises a tubular shaft having a central guidewire **lumen** and a helical rotor (148) extending at least partially over an exterior surface...

...2) a selective infusion-aspiration **catheter** comprising a **catheter** body having a proximal end, a distal end and a **lumen** between these, an impeller rotatable within the **lumen** of the **catheter** body and a driver coupled to the impeller to selectively rotate the impeller in a first direction to induce aspiration through the **catheter** body **lumen** or in a second direction to induce infusion through the **catheter** body...

...3) a circulation **catheter** comprising a **catheter** body having a proximal end, a distal end and a **lumen** between these and a first impeller arranged in a **lumen** of the **catheter** body to aspirate materials from the distal end to the proximal end of the **catheter** body and a second impeller arranged in a **lumen** of the **catheter** body to infuse materials from the proximal end to the distal end of the **catheter** body...

...6) a method for transporting materials between a target site in a body **lumen** of a patient and a location external to the patient comprising ...

...a) introducing a distal end of a **catheter** to the target site over a guidewire and rotating; and...

...b) rotating a first impeller over a guidewire within a **lumen** of the **catheter** to transport material between the distal and proximal end of the **catheter** ; and...

...7) a kit comprising a **catheter** and instructions for its use...

...For use in/as medical devices such as **catheters** (claimed) for removing unwanted tissues such as **thrombus** , atheroma, fluids, polyps, cysts or other **obstructive** matter from body **lumens** such as **blood vessels** , ureters, bile ducts or fallopian tubes. The material transport **catheters** may be used to **infuse** **thrombolytic** and other therapeutic agents and/or aspirate fragmented clot, **thrombus** and other **occlusive** materials in conjunction with **angioplasty** , atherectomy, laser ablation, embolectomy, endarterectomy and other **intravascular** interventions...

...The **catheter** efficiently evacuates the fragmented material from the **blood vessel** or body **lumen** , with continuous fluid infusion. Larger particles of fragmented material can be aspirated within a short...

...achievable using one rotor and the coiled rotors allow for the provision

of different fluid **flow rates** to different portions of the **catheter** . The impeller and rotor provide two different streams of the same or different materials to a single or multiple locations within the **catheter** . Two different fluids (chemicals and reagent that cannot be premixed prior to delivery) can also be mixed in situ at the distal end of the **catheter** . Use of a single impeller with a bi-directional flow allows circulation and recirculation of material to a target side within a patient body **lumen** to be achieved...

...The figure shows the partially broken, detailed view of distal end of the clot disruption **catheter** and mechanical pump...
... **Catheter** body (112...

... **Lumen** (130
Technology Focus:
... Preferred **Catheters** : The over-the-wire material transport, selective infusion-aspiration and circulation **catheters** further comprise a material capture device disposed at the distal end of the **catheter** body. The material capture device comprises a funnel structure, a macerator (140) and an expansible...

...portion of an inner surface of the expansible cage. Alternatively, the distal end of the **catheter** body is substantially free from surrounding structure. For the circulation **catheter** , the first impeller is disposed in a first **lumen** of the **catheter** body and the second impeller is disposed in a second **lumen** of the **catheter** body. The first and second impellers each comprise a shaft having a helical rotor (148) extending at least partially over an exterior surface and the **catheter** further comprises a tubular shaft. The first impeller comprises a first helical rotor extending at...

...comprises a second helical rotor extending at least partially over an inner surface of the **lumen** .
...

...further comprises a second coiled rotor element disposed over an inner surface of the central **lumen** of the inner tube. The first and second coiled rotors are counterwound or, alternatively, co...

...Preferred Transporting Method: The method for transporting materials between a target site in a body **lumen** of a patient and a location external to the patient further comprises applying a vacuum to a **lumen** of the **catheter** to assist in transporting material from the distal end. The impeller is selectively rotated to transport material from the distal end to the proximal end of the **catheter** or from the proximal end to the distal end of the **catheter** . The method also comprises delivering the material to be transported to the **catheter lumen** under pressure to assist in transporting material through the **catheter lumen** to the distal end of the **catheter** . The impeller is selectively rotated to infuse material to the body **lumen** at one time and selectively rotated to aspirate material from the body **lumen** at another time. The method further comprises rotating a second impeller in the **catheter** body to selectively transport material from the proximal end of the **catheter** to the distal end simultaneously with the transport of material to the proximal end from the distal end of the **catheter** , so that a circulation of material is established. The first and second impellers are counterwound...

...The method for selectively infusing and aspirating material between a target site in a body **lumen** of a patient and a location external to the patient preferably comprisesa) introducing a distal end of a **catheter** to the target site...

...b) rotating an impeller within a **lumen** of the **catheter** in a first direction to aspirate material from the target site; and...

...The method for selectively infusing and aspirating material through a target site in a body **lumen** of a patient preferably comprises...

...a) introducing a distal end of a **catheter** to the target site...

...b) rotating a first impeller within a **lumen** of the **catheter** to transport material to the target site; and...

...c) rotating a second impeller within a **lumen** of the **catheter** to transport material away from the target site...
...The first and second impellers are located in separate **lumens** within the **catheter** or, alternatively, within the same **lumen** within the **catheter** . When the first and second impellers are located within the same **lumen** within the **catheter** , the impellers comprise a flexible inner tube having a first helical rotor formed over an...
...Title Terms: **LUMEN** ;

22/5,K/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013750721 **Image available**
WPI Acc No: 2001-234950/200124
XRAM Acc No: C01-070347
XRPX Acc No: N01-168024
Pressure-based lumen **mapping apparatus for e.g.,** stenosis **identification by set of pressure measurements, comprises pressure wire, pressure sensor, pull back mechanism, and processor**
Patent Assignee: FLORENCE MEDICAL LTD (FLOR-N)
Inventor: BARAK C; DGANY E; NOSKOWICZ S H; SHALMAN E
Number of Countries: 094 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200113779	A2	20010301	WO 2000IL508	A	20000824	200124	B
AU 200067222	A	20010319	AU 200067222	A	20000824	200136	

Priority Applications (No Type Date): US 99155110 P 19990922; US 99150567 P 19990825
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200113779	A2	E	78	A61B-000/00	
AU 200067222	A			A61B-000/00	Based on patent WO 200113779

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

Abstract (Basic): WO 200113779 A2
NOVELTY - A pressure-based **lumen** mapping apparatus includes:
(i) a pressure wire for insertion to the **lumen** ;
(ii) a pressure sensor connected to the pressure wire for measuring pressure inside the **lumen** ;
(iii) a pull back mechanism for moving the pressure wire in predetermined manner; and
(iv) a processor for processing the pressure measurements
DETAILED DESCRIPTION - A pressure-based **lumen** mapping apparatus comprises:
(i) a pressure wire (60) for insertion to the **lumen** ;
(ii) a pressure sensor (40) connected to the pressure wire for measuring pressure inside the **lumen** ;
(iii) a pull back mechanism (50) for moving the pressure wire in predetermined manner; and
(iv) a processor for processing the pressure measurements to obtain parameters of fluid dynamics equation.
The pressure is measured at various points during the movement of the pressure wire.
The processor uses the pressure measurement to inversely obtain

22/5,K/5 (Item 5 from file: 350)
DIALOG(R)File 350:Derwent WPIX

013750721 **Image available**
WPI Acc No: 2001-234950/200124
XRAM Acc No: C01-070347
XRPX Acc No: N01-168024
Pressure-based lumen **mapping apparatus for e.g.,** stenosis **identification by set of pressure measurements, comprises pressure wire, pressure sensor, pull back mechanism, and processor**
Patent Assignee: FLORENCE MEDICAL LTD (FLOR-N)
Inventor: BARAK C; DGANY E; NOSKOWICZ S H; SHALMAN E
Number of Countries: 094 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200113779	A2	20010301	WO 2000IL508	A	20000824	200124	B
AU 200067222	A	20010319	AU 200067222	A	20000824	200136	

Priority Applications (No Type Date): US 99155110 P 19990922; US 99150567 P 19990825
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200113779	A2	E	78	A61B-000/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200067222	A		A61B-000/00	Based on patent WO 200113779

Abstract (Basic): WO 200113779 A2
NOVELTY - A pressure-based **lumen** mapping apparatus includes:
(i) a pressure wire for insertion to the **lumen** ;
(ii) a pressure sensor connected to the pressure wire for measuring pressure inside the **lumen** ;
(iii) a pull back mechanism for moving the pressure wire in predetermined manner; and
(iv) a processor for processing the pressure measurements
DETAILED DESCRIPTION - A pressure-based **lumen** mapping apparatus comprises:
(i) a pressure wire (60) for insertion to the **lumen** ;
(ii) a pressure sensor (40) connected to the pressure wire for measuring pressure inside the **lumen** ;
(iii) a pull back mechanism (50) for moving the pressure wire in predetermined manner; and
(iv) a processor for processing the pressure measurements to obtain parameters of fluid dynamics equation.
The pressure is measured at various points during the movement of the pressure wire.
The processor uses the pressure measurement to inversely obtain parameters of a fluid dynamics equation for mapping the **lumen** .
An INDEPENDENT CLAIM is also included for a method of pressure-based **lumen** mapping by:
(a) inserting a pressure wire with pressure sensor to the **lumen** ;
(b) moving the pressure wire from one point to another point along the **lumen** , while simultaneously measuring the pressure; and
(c) using the pressure measurement obtained during the movement, obtaining parameters of a fluid dynamics equation to provide at least one parameter of the **lumen** .
USE - The apparatus is used for:
(1) **stenosis** identification by set of pressure measurements;
(2) **stenosis** localization in the **artery** ;
(3) determining length, minimal diameter, and severity of **stenosis** ;
(4) hemodynamic reconstruction of **stenosis** geometry;
(5) calculating average **flow rate** in the **occluded artery** ;

(6) determination of average blood velocity; and
(7) determination of pulsatile index from the known flow in the **artery** .
The above data are essential for optimal selection of stent or **balloon** for the required **inflated** pressure and contact area, and for **drug delivery** .
DESCRIPTION OF DRAWING(S) - The figure is a schematic isometric view of the pressure-based **lumen** mapping apparatus.
Pressure sensor (40)
Pull back mechanism (50)
Pressure wire (60)
pp; 78 DwgNo 1/33

Title Terms: PRESSURE; BASED; **LUMEN** ; MAP; APPARATUS; **STENOSIS** ; IDENTIFY ; SET; PRESSURE; MEASURE; COMPRISE; PRESSURE; WIRE; PRESSURE; SENSE; PULL ; BACK; MECHANISM; PROCESSOR
Derwent Class: B07; P31
International Patent Class (Main): A61B-000/00
File Segment: CPI; EngPI

Pressure-based lumen **mapping apparatus for e.g.,** stenosis **identification by set of pressure measurements, comprises pressure wire, pressure sensor, pull back mechanism, and...**

Abstract (Basic):
... A pressure-based **lumen** mapping apparatus includes...

...i) a pressure wire for insertion to the **lumen** ;
(...

...ii) a pressure sensor connected to the pressure wire for measuring pressure inside the **lumen** ;
(
... A pressure-based **lumen** mapping apparatus comprises...

...i) a pressure wire (60) for insertion to the **lumen** ;
(...

...ii) a pressure sensor (40) connected to the pressure wire for measuring pressure inside the **lumen** ;
(...

...the pressure measurement to inversely obtain parameters of a fluid dynamics equation for mapping the **lumen** .
...
...An INDEPENDENT CLAIM is also included for a method of pressure-based **lumen** mapping by...

...a) inserting a pressure wire with pressure sensor to the **lumen** ;
(...

...b) moving the pressure wire from one point to another point along the **lumen** , while simultaneously measuring the pressure; and...

...obtaining parameters of a fluid dynamics equation to provide at least one parameter of the **lumen** .
...

...1) **stenosis** identification by set of pressure measurements...

...2) **stenosis** localization in the **artery** ;
(...

...3) determining length, minimal diameter, and severity of **stenosis** ;
(...

...4) hemodynamic reconstruction of **stenosis** geometry...
...5) calculating average **flow rate** in the **occluded artery** ;
(...

...7) determination of pulsatile index from the known flow in the **artery** .
...

...The above data are essential for optimal selection of stent or **balloon** for the required **inflated** pressure and contact area, and for **drug delivery** .
...

...The figure is a schematic isometric view of the pressure-based **lumen** mapping apparatus
Technology Focus:
... Preferred Parameters: The **lumen** map includes...

...1) geometrical parameter including minimal diameter of the **lumen** , length of **stenosis** , and percent area of **stenosis** ;
(...

...4) location of **stenosis** .
...
...Preferred Component: The pressure wire is guide wire or **catheter** .
...Title Terms: **LUMEN** ;

22/5,K/6 (Item 6 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012793966
WPI Acc No: 1999-600195/199951
Related WPI Acc No: 1999-518523
XRAM Acc No: C99-174650
XRPX Acc No: N99-442375
Inhibition of restenosis **by local application of e.g. hydrogen peroxide, thus avoiding use of radiation therapy**
Patent Assignee: SCIMED LIFE SYSTEMS INC (SCIM-N)
Inventor: HASTINGS R N; UNGS M T; URICK M J; WANG L; YANG D
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 5951458	A	19990914	US 96608655	A	19960229	199951	B
			US 97782471	A	19970110		
			US 97812248	A	19970306		
			US 97868482	A	19970603		
			US 97905296	A	19970801		

Priority Applications (No Type Date): US 97905296 A 19970801; US 96608655 A 19960229; US 97782471 A 19970110; US 97812248 A 19970306; US 97868482 A 19970603
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5951458	A		24	A61M-005/00	CIP of application US 96608655
					CIP of application US 97782471
					CIP of application US 97812248
					CIP of application US 97868482
					CIP of patent US 5855546
					CIP of patent US 5882290

Abstract (Basic): US 5951458 A
NOVELTY - **Restenosis** of **blood vessels** is inhibited by local application of an oxidizing agent, hydroxyl ions or a free radical generating agent.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(A) inhibiting **restenosis** of a **blood vessel** wall, comprising locally applying an oxidizing agent to the vessel walls;
(B) inhibiting **restenosis** of a **blood vessel** wall, comprising locally applying a free radical generating agent to the vessel walls; and

(C) inhibiting **restenosis** of a **stenosed coronary** vessel region, comprising locally applying hydroxyl ions to the vessel region.

ACTIVITY - Vasotropic; antirestenosis.

MECHANISM OF ACTION - None given.

USE - The processes are useful for preventing **restenosis** of **blood vessels** , especially **coronary arteries** .

ADVANTAGE - Local delivery of oxidizing agent avoids the need for the specialized equipment and personnel associated with use of radiation to prevent **restenosis** .

pp; 24 DwgNo 0/23

Title Terms: INHIBIT; LOCAL; APPLY; HYDROGEN; PEROXIDE; AVOID; RADIATE; THERAPEUTIC

Derwent Class: B06; B07; P34

International Patent Class (Main): A61M-005/00

File Segment: CPI; EngPI

Inhibition of restenosis **by local application of e.g. hydrogen peroxide, thus avoiding use of radiation therapy**

Abstract (Basic):

... **Restenosis** of **blood vessels** is inhibited by local application of an oxidizing agent, hydroxyl ions or a free radical

... A) inhibiting **restenosis** of a **blood vessel** wall, comprising locally applying an oxidizing agent to the vessel walls...

...B) inhibiting **restenosis** of a **blood vessel** wall, comprising locally applying a free radical generating agent to the vessel walls; and...

...C) inhibiting **restenosis** of a **stenosed coronary** vessel region, comprising locally applying hydroxyl ions to the vessel region...

...The processes are useful for preventing **restenosis** of **blood vessels** , especially **coronary arteries** .

...

...the need for the specialized equipment and personnel associated with use of radiation to prevent **restenosis** .

Technology Focus:

... especially less than 10) minutes. The active agent may be applied using a substance delivery **catheter** which has an elongate shaft including a distal region and an **inflatable balloon** disposed near the distal region. The **balloon** includes a perfusion **lumen** such that, when the **balloon** is **inflated** , blood perfuses through the **lumen** . The elongate shaft may include a **lumen** extending to the distal region, with the agent being forced through this **lumen** into the distal region. Alternatively, the active agent is applied to the external surface of the **balloon** prior to inserting the **balloon** into a patient. The oxidizing agent can be delivered either alone or in combination with...

Extension Abstract:

... Test sites in pig **coronary arteries** were injured by expansion of an over-sized **balloon** followed by stent placement. Two or three sites in each of four animals were injured...

...with various concentrations of hydrogen peroxide for various lengths of time. The hydrogen peroxide was **delivered** locally to the stented site using a **drug delivery catheter** .

...

...and a 1% solution was infused for 20 minutes, at a rate of 0.5 **cc** /minute. Control animals had an average diameter reduction of 36% when examined 30 days post

22/5,K/7 (Item 7 from file: 350)

DIALOG(R)File 350:Derwent WPIX

010742331 **Image available**
WPI Acc No: 1996-239286/199624
XRAM Acc No: C96-076341
XRPX Acc No: N96-200305
Device for infusing agent adjacent to blood vessel **wall - has ports in distal segment which can be formed into expanded helical coil to leave high** flow rate **central** lumen
Patent Assignee: MICRO THERAPEUTICS INC (MICR-N)
Inventor: CRAGG A H; EVANS S M; WALLACE G B; CRAGG M D A H
Number of Countries: 019 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9613295	A1	19960509	WO 95US13414	A	19951018	199624	B
CA 2160847	A	19960421	CA 2160847	A	19951018	199634	
US 5554114	A	19960910	US 94326609	A	19941020	199642	
EP 787018	A1	19970806	EP 95938787	A	19951018	199736	
			WO 95US13414	A	19951018		
JP 10509350	W	19980914	WO 95US13414	A	19951018	199847	
			JP 96514640	A	19951018		

Priority Applications (No Type Date): US 94326609 A 19941020
Cited Patents: US 5116309
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9613295	A1	E	31	A61M-025/00	
Designated States (National): JP					
Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
US 5554114	A		13	A61M-025/00	
EP 787018	A1	E		A61M-025/00	Based on patent WO 9613295
Designated States (Regional): BE DE FR GB IT NL					
JP 10509350	W		35	A61M-025/00	Based on patent WO 9613295
CA 2160847	A			A61M-025/01	

Abstract (Basic): WO 9613295 A

Device for **infusing** a **drug** or other agent into a peripheral low blood **flow rate** region adjacent to a **blood vessel** wall comprises a tube with infusion ports (18) along and around a distal segment (26) following a proximal straight segment. The distal segment can be formed into an expanded helical coil of not less than 2 turns leaving a central higher **flow rate lumen** . In the coil, the ports face the vessel wall, adjacent coil turns and the central **lumen** . The distal segment pref. has a sheath around a coiled wire and is biased towards expanded state so that it can be contracted by a core wire for advancement and expand when the wire is withdrawn.

USE - E.g. to deliver a lytic agent to a **blood clot** , or an agent to a vessel wall after **angioplasty** .

ADVANTAGE - Permits simpler and less expensive **drug delivery** to a vessel wall or **obstruction** while allowing the blood to flow centrally.

Dwg.1/13

Title Terms: DEVICE; INFUSION; AGENT; ADJACENT; BLOOD; VESSEL; WALL; PORT; DISTAL; SEGMENT; CAN; FORMING; EXPAND; HELICAL; COIL; LEAVE; HIGH; FLOW; RATE; CENTRAL; **LUMEN**
Derwent Class: B07; P34
International Patent Class (Main): A61M-025/00; A61M-025/01
International Patent Class (Additional): A61M-025/09
File Segment: CPI; EngPI

Device for infusing agent adjacent to blood vessel **wall...**

...ports in distal segment which can be formed into expanded helical coil to leave high flow rate **central** lumen

...Abstract (Basic): Device for **infusing** a **drug** or other agent into a peripheral low blood **flow rate** region adjacent to a **blood vessel** wall comprises a tube with infusion ports (18) along and around a

distal segment (26...

...into an expanded helical coil of not less than 2 turns leaving a central higher **flow rate lumen** . In the coil, the ports face the vessel wall, adjacent coil turns and the central **lumen** . The distal segment pref. has a sheath around a coiled wire and is biased towards...

...USE - E.g. to deliver a lytic agent to a **blood clot** , or an agent to a vessel wall after **angioplasty** .
...

...ADVANTAGE - Permits simpler and less expensive **drug delivery** to a vessel wall or **obstruction** while allowing the blood to flow centrally
...Abstract (Equivalent): A method for introducing a **drug** or agent into a desired **infusion** site in a **blood vessel** and for **infusing** a **drug** or agent into the **blood vessel** in the peripheral low blood **flow rate** region thereof comprising the steps of...

...segment and a proximal segment and a proximal and distal end and having an infusion **lumen** formed therein extending along the axis of the elongated tubular body from the proximal end...

...and outwardly from the proximal segment when positioned at a desired infusion site in a **blood vessel** , the expanded helical coil infusion configuration providing a generally centrally disposed higher **flow rate** perfusion **lumen** for perfusing blood centrally therethrough and locating the plurality of infusion ports in the peripheral low blood **flow rate** region of the **blood vessel** , such that at least said first portion of the plurality of infusion ports face outward...

...and said third portion of the plurality of infusion ports face inward toward the perfusion **lumen** ;
...

...segment for facilitating advancement of said distal infusion segment to a selected location in a **blood vessel** ;
...

...advancing said infusion device with said straightened distal infusion segment through the patient's **vascular** system to located said distal infusion segment at a desired site in a **blood vessel**
...
...introducing an infusion fluid into the **lumen** for infusion through said plurality of infusion ports in the low blood **flow rate** region adjacent to said **blood vessel** wall
...Title Terms: **LUMEN**
?

```
Set     Items   Description
S1     125105   (VENOUS OR VEIN? OR ARTERY OR ARTERI? OR VASCULAR? OR INTR-
            ?VASC? OR INTR?VEN? OR BLOOD?()VESSEL? OR VENAL OR CORONAR?)
S2     209186   OCCLUD? OR OCCLUSI? OR OBSTRUCT? OR STENOS? OR STENOT? OR -
            RESTENOS? OR RESTENOT? OR PLAQUE?
S3      59221   SCLERO? OR THROMB? OR BLOODCLOT? OR BLOOD()CLOT? OR ISCHEM-
            I? OR ARTER?SCLER? OR PLAQUING
S4        477   CALCIUM()DEPOSIT?
S5      45136   BALLOON? OR PLASTY? OR PLASTIE? ? OR ANGIOPLAST? OR OCCLU?-
            ()DEVICE? OR INFLAT? OR CARDIOPLAST?
S6         25   ARTERIOPLAST?
S7     506183   DELIVER? OR ADMINIST? OR INJECT? OR INFUS? OR PERFUS?
S8      56785   CATHETER? OR CANNULA? OR CANULA? OR TROCAR? OR LUMEN? OR H-
            OLLOW?(N)WIRE?
S9     127486   DRUG? OR NARCOTIC? OR OCCLU?(N)TREAT? OR ANTICOAGUL? OR AN-
            TI()COAGUL? OR THROMBIT?
S10     23096   RADIONUCLID? OR RADIO()NUCLID? OR RADIOISOTOP? OR RADIO()I-
            SOTOP? OR RADIOACTIVE()ISOTOP?
S11        77   RADIO()ACTIVE()ISOTOP?
S12    174646   FLOWRATE? OR FLOW()RATE? OR "CC" OR "C.C." OR CUBIC()CENTI-
            L?
S13     56815   S7(10N)(S9 OR S10 OR S11)
S14      3360   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6) AND S8 AND S12
S15      1997   S13 AND S14
S16   1327567   1(10N)(S2 OR S3 OR 4)
S17      8963   S16(S)(S5 OR S6)
S18     56815   S7(10N)(S9 OR S10 OR S11)
S19         0   S 16 AND S17 AND S18
S20      2135   S16 AND S17 AND S18
S21      1593   S20 AND S8
S22       777   S21 AND S12
S23   1373959   PY<1999
S24       179   S22 AND S23
?
?show files
File 348:EUROPEAN PATENTS 1978-2003/Sep W03
         (c) 2003 European Patent Office
File 349:PCT FULLTEXT 1979-2002/UB=20030925,UT=20030918
         (c) 2003 WIPO/Univentio
?
```

24/5,K/41 (Item 5 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00464714 **Image available**

PERFUSION BALLOON AND RADIOACTIVE WIRE DELIVERY SYSTEM
BALLONNET DE PERFUSION ET DISPOSITIF D'ADMINISTRATION A FIL RADIOACTIF

Patent Applicant/Assignee:
SCIMED LIFE SYSTEMS INC,
Inventor(s):
HASTINGS Roger N,
URICK Michael J,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9855179 A1 **19981210**
Application: WO 98US10235 19980519 (PCT/WO US9810235)
Priority Application: US 97482 19970603
Designated States: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61N-005/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 10450

English Abstract
This invention is a **catheter** (320) capable of irradiating blood vessel walls to inhibit restenosis after angioplasty. **Catheters** (320) are capable of simultaneous irradiation, angioplasty, and in some devices **drug infusion** . Preferred **catheters** (320) include a helical **perfusion** balloon (336) having strand windings (346) spaced apart when inflated, and defining a perfusion **lumen** (356) within. A tubular sheath (374) over the helical strands (346), and distal shaft region (326) is used in some embodiments and defines an outer wall for the perfusion **lumen** (356). A spiral, inter-strand space (376) is defined between the sheath outer wall, and the blood vessel inner wall providing a confined volume for controlled **delivery** of **drugs** to the vessel wall in conjunction with irradiation. A device having a radiation wire distally closed end tube is provided. A device having a radiation wire open ended tube terminating proximally of the perfusion **lumen** is also provided.

French Abstract
L'invention concerne un **catheter** (32 parois du vaisseau sanguin pour inhiber une rest stie. Les **catheters** (320) de l'invention peuver e irradiation, une angioplastie et, dans ne infusion de medicaments. Des **catheters** prefer lonnet de perfusion (336) muni d'enroulements de que le ballonnet est gonfle et delimitant une 56) placee a l'interieur. Une gaine tubulaire (37 pirales (346) et une partie de manchon distale certaines formes de realisation et delimite une paroi externe pour la lumiere de perfusion (356). Un espace spirale (376) entre les fils est delimite entre la paroi externe de la gaine et la paroi interne du vaisseau sanguin et presente un volume captif pour combiner un apport regule de medicaments a la paroi vasculaire et une irradiation. L'invention concerne en outre un dispositif comprenant un tube terminal a fil radioactif et fermeture distale; elle concerne enfin un dispositif comprenant un tube extensible a fil radioactif arrivant a proximite de la lumiere de perfusion.

most promising reference of full for Patent File (expanded)

Patent and Priority Information (Country, Number, Date):
Patent: ... **19981210**
Fulltext Availability:
Detailed Description
Claims

English Abstract
This invention is a **catheter** (320) capable of irradiating blood vessel

walls to inhibit restenosis after angioplasty. **Catheters** (320) are capable of simultaneous irradiation, angioplasty, and in some devices **drug infusion** . Preferred **catheters** (320) include a helical **perfusion** balloon (336) having strand windings (346) spaced apart when inflated, and defining a perfusion **lumen** (356) within. A tubular sheath (374) over the helical strands (346), and distal shaft region (326) is used in some embodiments and defines an outer wall for the perfusion **lumen** (356). A spiral, inter-strand space (376) is defined between the sheath outer wall, and the blood vessel inner wall providing a confined volume for controlled **delivery** of **drugs** to the vessel wall in conjunction with irradiation. A device having a radiation wire distally ...

...provided. A device having a radiation wire open ended tube terminating proximally of the perfusion **lumen** is also provided.

French Abstract

L'invention concerne un **catheter** (320) pouvant irradier les parois du vaisseau sanguin pour inhiber une restenose apres une angioplastie. Les **catheters** (320) de l'invention peuvent a la fois effectuer une irradiation, une angioplastie et, dans certains dispositifs, une infusion de medicaments. Des **catheters** preferes (320) incluent un ballonnet de perfusion (336) muni d'enroulements de fils (346) espaces...

Publication Year: **1998**

Detailed Description

... by reference. This application is related to U.S. Patent No. 5,558,642, entitled **DRUG DELIVERY CATHETER** , also incorporated by reference.

Field of the Invention

The present invention relates generally to intralumenal or intravascular **catheters** used 5 to delivery radiation inside a living body. More specifically, the present invention relates to radioactive perfusion balloon **catheters** for therapeutic purposes.

Background of the Invention

Intravascular diseases are cominonly treated by relatively non...

...known in the art and typically involve use of a guide wire and a balloon **catheter** , possibly in combination with other intravascular devices. A typical balloon **catheter** has an elongate shaft with a balloon attached to its distal end and a manifold attached to the proximal end. In use, the balloon **catheter** is advanced over the guide wire such that the balloon is positioned adjacent a restriction...

...be in part a healing response to the dilation, including the formation of scar tissue.

Drug infusion near the stenosis has been proposed as a means to inhibit restenosis.

0 U.S. Patent No. 5,558,642 to Schweich, Jr. et al. describes **drug delivery** devices and methods for **delivering** pharmacological agents to vessel walls in conjunction with angioplasty.

Intravascular radiation, including thermal, light and...

...No. 4,799,479 to Spears suggests that heating a dilated restriction may prevent gradual 1 5 **restenosis** at the dilation site. In addition, U.S. Patent No. 5,417,653 to Sahota...simultaneously dilating a stenosis and delivering radioactive radiation.

in particular, Verin discloses a balloon dilatation **catheter** having an open-ended **lumen** extending therethrough for the delivery of a radioactive guide wire.

One problem associated with the open-ended **lumen** design is that bodily fluids (e.g., blood) may come into contact with the radioactive...

...5,503,613 to Weinberger et al. proposes the use of a separate closed-ended **lumen** in a balloon **catheter** . The closed-ended lunien may be used to deliver a radioactive guide wire without the...

...ended himen design also has draw backs. For example, the addition of a separate delivery **lumen** tends to increase the overall profile of the **catheter** . An increase in profile is not desirable because it may reduce **flow rate** of fluid injections into the guide **catheter** and it may interfere with navigation in small vessels.

1 5 Another problem with both...

...of restenosis. Dake et al. suggest delivering radiation within the distal portion of a tubular **catheter** . Fischell, in the publication EPO 0 593 136 Al, suggests placing a thin wire having...5,540,659 to Tierstein suggests use of a helical centering balloon, attached to a **catheter** at points about the radiation source to allow perfusion through the balloon, between the balloon...

...radiation to vessel interiors to inhibit restenosis. What remains to be provided is an improved **perfusion catheter** having radiation **delivery** and **drug infusion** capabilities.

Sumniga of the Invention
The present invention includes devices and methods for providing radiation...

...The preferred device includes a balloon assembly disposed at the distal region 0 of a **catheter** shaft, where the **catheter** shaft includes an inflation **lumen** , a radiation wire **lumen** , and a **drug infusion lumen** . In the distal region, the radiation wire **lumen** can be disposed above the shaft, making room for a distal, single-operator-exchange guide wire **lumen** . The spiral, inflatable windings are laced inside shaft through- holes transverse to the shaft longitudinal...

...the strands also provides positions along the shaft in between windings for the placement of **drug infusion** apertures. Preferred devices include a tubular sheath over the helical balloon and shaft distal region, defining a perfusion **lumen** outer wall. The sheath preferably is snugly attached to both the exterior contours of the individual helical balloon strand windings and the **catheter** shaft.
2 0 One sparsely wound device includes a closed end radiation tube extending through...

...device allows for use and re-use of non-sterilized radiation sources with the sterile **catheter** . Another device includes an open ended radiation tube terminating distally near the proximal end of...

...wire or source through the balloon, without having a radiation wire tube within the perfusion **lumen** within the balloon.

The open ended radiation wire tube embodiment provides greater perfusion cross-sectional...

...area. The open ended embodiment can also provide a smaller, uninflated profile.

In devices supporting **drug infusion** , **drug infusion** apertures extend through the **catheter** shaft distal region between balloon strand windings. The **infused drug** exits the apertures into the inter-strand spaces outside the tubular sheath and contacts the inside of the enclosing blood vessel wall. The **drug** can spread around the outside of the **perfusion** sheath 0 through the spiral shaped spaces created by the helical strand windings underneath the tubular sheath material. The confined space allows concentrated **drug delivery** against the vessel wall.

24/5/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00974215
Methods for treating thrombotic disorders
Methoden zur Behandlung thrombothischer Storungen
Methodes de traitement de problemes thrombotiques
PATENT ASSIGNEE:
ELI LILLY AND COMPANY, (204942), Lilly Corporate Center, Indianapolis, Indiana 46285, (US), (Applicant designated States: all)
INVENTOR:
Grinnell, Brian William, 3625 East 71st Street, Indianapolis, Indiana 46220, (US)
Jakubowski, Joseph Anthony, 3740 Governors Road, Indianapolis, Indiana 46208, (US)
LEGAL REPRESENTATIVE:
Denholm, Anna Marie et al (78623), Eli Lilly and Company Limited, Lilli Research Centre, Erl Wood Manor, Windlesham Surrey GU20 6PH, (GB)
PATENT (CC, No, Kind, Date): EP 882453 A2 981209 (Basic)
EP 882453 A3 010404
APPLICATION (CC, No, Date): EP 98304327 980602;
PRIORITY (CC, No, Date): US 48628 970605
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; RO; SI
INTERNATIONAL PATENT CLASS: A61K-038/48; A61K-039/395; A61P-007/02; A61K-038/48; A61K-31:60; A61K-31:435; A61K-038/48; A61K-31:60; A61K-31:505; A61K-038/48; A61K-31:60; A61K-31:34; A61K-039/395; A61K-38:48; A61K-31:60; A61K-038/48; A61K-31:60; A61K-038/48; A61K-31:34; A61K-039/395; A61K-38:48

ABSTRACT EP 882453 A2
The present invention provides a method of treatment for patients with a variety of thrombotic disorders including, but not limited to, stroke, venous thrombosis, myocardial infarction, unstable angina, abrupt closure following angioplasty or stent placement, and thrombosis as a result of peripheral vascular surgery. Said treatment is a combination therapy with human aPC and antiplatelet agents including, but not limited to, aspirin (ASA), clopidogrel, ReoPro(R) (abciximab), dipyridamole, ticlopidine and IIb/IIIa receptor antagonists. The synergy will result in the ability to reduce the dosages of the agents used in the combination therapy.
ABSTRACT WORD COUNT: 92

LEGAL STATUS (Type, Pub Date, Kind, Text):

Change:	010404	A2	International Patent Classification changed: 20010214
Application:	981209	A2	Published application (A1with Search Report ;A2without Search Report)
Extended:	020102	A2	Extended states: AL; LT; LV; RO; SI
Change:	010718	A2	Legal representative(s) changed 20010528
Search Report:	010404	A3	Separate publication of the search report
Change:	010418	A2	Legal representative(s) changed 20010227
Examination:	011031	A2	Date of dispatch of the first examination report: 20010917
Examination:	981209	A2	Date of filing of request for examination: 980608

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9850	261
SPEC A	(English)	9850	4071
Total word count - document A			4332
Total word count - document B			0
Total word count - documents A + B			4332

24/5/20 (Item 20 from file: 348)

00705606
An intravascular drug delivery system
Vorrichtung zur Arzneimittelverabreichung in Blutgefassen
Systeme intravasculaire pour l'administration de medicaments
PATENT ASSIGNEE:
SCHNEIDER (USA) INC., (811409), 5905 Nathan Lane, Plymouth, Minnesota 55442, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;NL;PT;SE)
INVENTOR:
GOODIN, Richard, L., 940 127th Lane N.E., Blaine, MN 55434, (US)
LEGAL REPRESENTATIVE:
Walters, Frederick James et al (37251), Urquhart-Dykes & Lord 91 Wimpole Street, London W1M 8AH, (GB)
PATENT (CC, No, Kind, Date): EP 732958 A1 960925 (Basic)
EP 732958 B1 990217
WO 9515782 950615
APPLICATION (CC, No, Date): EP 94928502 941014; WO 94IB316 941014
PRIORITY (CC, No, Date): US 163852 931207
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61M-025/10; A61M-029/02;
NOTE:
No A-document published by EPO
LEGAL STATUS (Type, Pub Date, Kind, Text):

Lapse:	000524	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217,
Oppn None:	20000202	B1 No opposition filed: 19991118
Lapse:	020626	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217, BE 19990217, CH 19990217, LI 19990217, ES 19990217, GR 19990217, PT 19990517, SE 19990217,
Lapse:	010606	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217, BE 19990217, CH 19990217, LI 19990217, GR 19990217, PT 19990517,
Lapse:	001213	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217, BE 19990217, CH 19990525, LI 19990525, PT 19990517,
Lapse:	000607	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217, BE 19990217, PT 19990517,
Lapse:	001227	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217, BE 19990217, CH 19990217, LI 19990217, PT 19990517,
Lapse:	020605	B1 Date of lapse of European Patent in a contracting state (Country, date): AT 19990217, BE 19990217, CH 19990217, LI 19990217, GR 19990217, PT 19990517, SE 19990217,
Application:	950906	A International application (Art. 158(1))
Application:	960925	A1 Published application (A1with Search Report ;A2without Search Report)
Examination:	960925	A1 Date of filing of request for examination: 960528
Examination:	970709	A1 Date of despatch of first examination report: 970523
Change:	980107	A1 Representative (change)
Change:	980624	A1 Title of invention (German) (change)
Change:	980624	A1 Title of invention (English) (change)
Change:	980624	A1 Title of invention (French) (change)
Grant:	990217	B1 Granted patent

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9907	542
CLAIMS B	(German)	9907	545
CLAIMS B	(French)	9907	602
SPEC B	(English)	9907	3962

Total word count - document A 0
Total word count - document B 5651
Total word count - documents A + B 5651

24/5/27 (Item 27 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00445545
CONTINUOUS DRUG **SOLUTION** INJECTOR **EQUIPPED WITH BALLOON.**
INJEKTOR MIT BALLON ZUR KONTINUIERLICHEN INJEKTION EINER ARZNEIMITTELLOSUNG.
INJECTEUR CONTINU DE SOLUTION MEDICAMENTEUSE EQUIPE D'UN BALLON.
PATENT ASSIGNEE:
TSUKADA MEDICAL RESEARCH CO., LTD., (1232000), 8-12-504, Kitashinjuku 4-chome, Shinjuku-ku, Tokyo 169, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
TSUKADA, Osamu, 318-1, Ohazasumiyoshi, Ueda-shi, Naga no 380, (JP)
LEGAL REPRESENTATIVE:
Spall, Christopher John et al (36171), BARKER, BRETTELL & DUNCAN 138 Hagley Road, Edgbaston Birmingham B16 9PW, (GB)
PATENT (CC, No, Kind, Date): EP 473781 A1 920311 (Basic)
EP 473781 A1 920812
EP 473781 B1 951011
WO 9112835 910905
APPLICATION (CC, No, Date): EP 90903935 900228; WO 90JP266 900228
PRIORITY (CC, No, Date): EP 90903935 900228; WO 90JP266 900228
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61M-005/152;
CITED PATENTS (EP A): EP 295504 A; EP 172586 A
CITED PATENTS (WO A): JP 64070069 A; JP 56102252 A

ABSTRACT EP 473781 A1
This invention relates to a continuous **drug** solution **injector** equipped with a balloon and used for **injecting** a **drug** solution filled in a balloon made of an elastic material into the human body within a predetermined period of time by utilizing the shrinking force of the balloon. A bottomed cylinder (3) is fitted slidably with its bottom facing outward into a tubular body (1) which is formed by connectong a drug solution charge portion (5) having a valve member and a drug solution discharge portion (6) having a drug solution discharge control portion through a flow path change-over valve (4) disposed at an intermediate portion. A plurality of holes (12 or 31) are bored in the tubular body or the cylinder. The peripheral edges of the balloon (2) are fixed air-tight to both the tubular body and the cylinder in such a manner as to encompass the junction between the tubular body and the cylinder as well as the holes. Thus the cylinder can slide relative to the tubular body with the aid of the elasticity of the balloon and the inner pressure of the drug solution when the balloon undergoes expansion and shrinkage, and the balloon can undergo expansion and shrinkage in substantially the same quantity in the direction of the center axis in a longitudinal direction and an axial direction vertical to the former, whereby the **drug** solution can be **injected** uniformly without intermission. (see image in original document)
ABSTRACT WORD COUNT: 243

LEGAL STATUS (Type, Pub Date, Kind, Text):
Lapse: 020619 B1 Date of lapse of European Patent in a contracting state (Country, date): AT

		19951011, CH 19951011, LI 19951011, DK 19951011, ES 19951011, LU 19960229, SE 19960111,
Lapse:	20000209 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19951011, CH 19951011, LI 19951011, DK 19951011, LU 19960229, SE 19960111,
Lapse:	030212 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19951011, CH 19951011, LI 19951011, DK 19951011, ES 19951011, LU 19960229, NL 19951011, SE 19960111,
Application:	920311 A1	Published application (Alwith Search Report ;A2without Search Report)
Examination:	920429 A1	Date of filing of request for examination: 920227
Search Report:	920812 A1	Drawing up of a supplementary European search report: 920624
Examination:	940427 A1	Date of despatch of first examination report: 940310
Grant:	951011 B1	Granted patent
Lapse:	960605 B1	Date of lapse of the European patent in a Contracting State: SE 960111
Lapse:	960710 B1	Date of lapse of the European patent in a Contracting State: AT 951011, SE 960111
Oppn None:	961002 B1	No opposition filed
Lapse:	970326 B1	Date of lapse of the European patent in a Contracting State: AT 951011, CH 951011, LI 951011, SE 960111
Lapse:	970326 B1	Date of lapse of the European patent in a Contracting State: AT 951011, CH 951011, LI 951011, SE 960111
Lapse:	980408 B1	Date of lapse of the European patent in a Contracting State: AT 951011, CH 951011, LI 951011, DK 951011, SE 960111

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	238
SPEC A	(English)	EPABF1	4424
Total word count - document A			4662
Total word count - document B			0
Total word count - documents A + B			4662

24/5/29 (Item 29 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00396868
Catheter **and method for locally applying medication to the wall of a blood vessel or other body** lumen .
Katheter und Methode zur lokal angewandten Medikation der Wand eines Blutgefasses oder eines anderen Korperlumens.
Catheter et methode pour medication appliquee localement sur la paroi d'un vaisseau sanguin ou d'une autre cavite corporelle.
PATENT ASSIGNEE:
C.R. BARD, INC., (247301), 730 Central Avenue, Murray Hill New Jersey 07974, (US), (applicant designated states: DE;ES;FR;GB;IT;NL)
INVENTOR:
Wolinsky, Harvey, 49 East 96 Street, New York, NY 10128, (US)
Barbere, Michael D., 306 Groton Street, Dunstable, Massachusetts 01827, (US)
King, Spencer L., 95 Lullwater Parkway, Atlanta, Georgia 30307, (US)
LEGAL REPRESENTATIVE:
Woodward, John Calvin et al (37981), Venner Shipley & Co. 20 Little Britain, London EC1A 7DH, (GB)
PATENT (CC, No, Kind, Date): EP 383429 A2 900822 (Basic)

EP 383429 A3 910327
EP 383429 B1 951108
APPLICATION (CC, No, Date): EP 90300438 900116;
PRIORITY (CC, No, Date): US 304352 890131
DESIGNATED STATES: DE; ES; FR; GB; IT; NL
INTERNATIONAL PATENT CLASS: A61M-025/10; A61M-031/00; A61M-029/02;
CITED PATENTS (EP A): EP 338979 A; EP 338979 A; US 4490421 A; EP 284672 A; EP 284672 A; EP 205851 A

ABSTRACT EP 383429 A2

A method and **catheter** for use in practising the method are provided by which a highly concentrated medication or chemotherapeutic agent can be applied locally under sufficient pressure to cause the medication or agent to penetrate into the localized tissue. The total volume of medication or agent is quite small, well below levels that might cause an adverse reaction in other parts of the body. The **catheter** includes a thin walled flexible balloon (16) having a plurality of minute holes (29) through which medication may flow at a low **flow rate** . The balloon (16) is inflated with the medication under pressure and the low **flow rate** of the order of a few ccs per minute is controlled by the minute holes (29) in the balloon (16). In practising the method of the invention, the balloon (16) is selected such that its inflated diameter will correspond to or be slightly greater than the diameter of the **lumen** into which it is to be placed so that when the balloon (16) is inflated, it will contact intimately the surface of the **lumen** . Inflation of the balloon (16) with the medication will cause a thin film to spread between the balloon (16) and the **lumen** , the film being maintained under a sufficient pressure to penetrate significantly the surrounding tissue with a high concentration of medication. The quantity of medication that ultimately flows free into the **lumen** is quite small and is insufficient to cause any other damage to the patient.
ABSTRACT WORD COUNT: 249

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	900822 A2	Published application (A1with Search Report ;A2without Search Report)
Search Report:	910327 A3	Separate publication of the European or International search report
Change:	910529 A2	Obligatory supplementary classification (change)
Examination:	911009 A2	Date of filing of request for examination: 910802
Examination:	921216 A2	Date of despatch of first examination report: 921029
Grant:	951108 B1	Granted patent
Oppn None:	961030 B1	No opposition filed

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	490
CLAIMS B	(English)	EPAB95	601
CLAIMS B	(German)	EPAB95	614
CLAIMS B	(French)	EPAB95	616
SPEC A	(English)	EPABF1	2861
SPEC B	(English)	EPAB95	2877
Total word count - document A			3351
Total word count - document B			4708
Total word count - documents A + B			8059

24/5/33 (Item 33 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00312914
Retroperfusion and retroinfusion control apparatus, system and method.
Gerat, System und Verfahren zur Steuerung der Retroperfusion und Retroinfusion.

Appareil, systeme et procede pour la commande de retroperfusion et retro-infusion.

PATENT ASSIGNEE:
RETROPERFUSION SYSTEMS, INC., (981110), 3178 Pullman Avenue, Costa Mesa California 92626, (US), (applicant designated states: DE;FR;GB;IT;SE)
INVENTOR:
Lundquist, Ingemar H., 17 Miles Drive at Dunes Road, Pebble Beach California 93953, (US)
Tarczy-Hornoch, Zoltan, 7106 Marlborough Terrace, Berkeley California 94705, (US)
Kardos, Thomas J., 1570 Via Capri, No. 10, Laguna Beach California 92651, (US)
LEGAL REPRESENTATIVE:
Cross, Rupert Edward Blount et al (42891), BOULT, WADE & TENNANT 27 Furnival Street, London EC4A 1PQ, (GB)
PATENT (CC, No, Kind, Date): EP 297723 A2 890104 (Basic)
EP 297723 A3 890503
EP 297723 B1 930825
APPLICATION (CC, No, Date): EP 88304932 880531;
PRIORITY (CC, No, Date): US 56401 870529; US 120591 871113; US 198441 880525
DESIGNATED STATES: DE; FR; GB; IT; SE
INTERNATIONAL PATENT CLASS: A61M-001/10;
CITED PATENTS (EP A): US 4493697 A; US 4648384 A; FR 2458288 A; DE 3610255 A; US 4459977 A; GB 1444117 A

ABSTRACT EP 297723 A2
Retroperfusion control apparatus (11) for supplying arterial blood of a patient to the venous side of the patient's heart including a pump (81) having an inlet (104) and an outlet (114) and a piston (88) movable through a pump stroke for moving a liquid from the inlet (104) to the outlet (114) of the pump (81). A stepper motor (47) is provided which drives the piston (81). Electronic circuitry is provided for driving the stepper motor (47) and senses the presence of an R wave in a patient to operate the stepper motor (47) in response to the sensed R wave.
ABSTRACT WORD COUNT: 105

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	890104	A2	Published application (Alwith Search Report ;A2without Search Report)
Search Report:	890503	A3	Separate publication of the European or International search report
Examination:	900321	A2	Date of filing of request for examination: 891103
Examination:	900606	A2	Date of despatch of first examination report: 900424
Grant:	930825	B1	Granted patent
Lapse:	940420	B1	Date of lapse of the European patent in a Contracting State: SE 930825
Oppn None:	940817	B1	No opposition filed
Lapse:	991020	B1	Date of lapse of European Patent in a contracting state (Country, date): IT 19930825, SE 19930825,

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1050
CLAIMS B	(German)	EPBBF1	438
CLAIMS B	(French)	EPBBF1	510
SPEC B	(English)	EPBBF1	14787
Total word count - document A			0
Total word count - document B			16785
Total word count - documents A + B			16785

24/5/36 (Item 36 from file: 348)

4/5/36 (Item 36 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00292372
Liquid infusion device.
Flussigkeitsinjektionsvorrichtung.
Dispositif d'infusion de liquides.
PATENT ASSIGNEE:
NISSHO CORPORATION, (752510), 9-3, Honjo-nishi, 3-chome Oyodo-ku, Osaka-shi, (JP), (applicant designated states: BE;DE;FR;GB;IT;NL)
INVENTOR:
Tsujikawa, Hajime, 5-19, Hama-cho, Otsu-shi Shiga-ken, (JP)
Yoshida, Toshiki, 12-3-508, Aoba 3-chome Shimamoto-cho, Mishima-gun Osaka-fu, (JP)
LEGAL REPRESENTATIVE:
Turk, Gille, Hrabal (100971), Brucknerstrasse 20, W-4000 Dusseldorf 13, (DE)
PATENT (CC, No, Kind, Date): EP 295504 A2 881221 (Basic)
EP 295504 A3 890308
EP 295504 B1 910807
APPLICATION (CC, No, Date): EP 88108834 880602;
PRIORITY (CC, No, Date): JP 87152971 870618; JP 87204791 870817; JP 87294809 871120
DESIGNATED STATES: BE; DE; FR; GB; IT; NL
INTERNATIONAL PATENT CLASS: A61M-005/14;
CITED PATENTS (EP A): EP 172586 A; EP 172586 A; US 3961725 A; US 3469578 A; US 3469578 A; US 4121585 A; GB 1066739 A; GB 1066739 A; US 4140117 A; US 4140117 A; US 4031891 A; US 4031891 A

ABSTRACT EP 295504 A2
A liquid infusion device (I) comprising a bladder assembly (A) and a flow-regulating portion (C). The bladder assembly (A) comprises a tubular outer shaft (101), an inner shaft slidably (102) received within the outer shaft and a bladder (103) covering the outer and inner shafts. The bladder can inflate in both its radial and axial directions whereby reducing the residual amounts of liquid drug in the bladder on dispensation of liquid drug. The flow-regulating portion (C) comprises a pipe having at least one small hole or a pipe having a very small diameter, so that the accurate regulation of liquid drug can be performed.
ABSTRACT WORD COUNT: 108

LEGAL STATUS (Type, Pub Date, Kind, Text):
Application: 881221 A2 Published application (A1with Search Report ;A2without Search Report)
Search Report: 890308 A3 Separate publication of the European or International search report
Examination: 890614 A2 Date of filing of request for examination: 890407
Examination: 901128 A2 Date of despatch of first examination report: 901016
Grant: 910807 B1 Granted patent
Oppn None: 920729 B1 No opposition filed
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	556
CLAIMS B	(German)	EPBBF1	588
CLAIMS B	(French)	EPBBF1	655
SPEC B	(English)	EPBBF1	6507
Total word count - document A			0
Total word count - document B			8306
Total word count - documents A + B			8306

24/5/40 (Item 4 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00465050

MODIFIED LOW MOLECULAR WEIGHT HEPARIN THAT INHIBITS CLOT ASSOCIATED COAGULATION FACTORS

HEPARINE DE FAIBLE POIDS MOLECULAIRE MODIFIEE INHIBANT LES FACTEURS DE COAGULATION ASSOCIES AU CAILLOT

Patent Applicant/Assignee:
HAMILTON CIVIC HOSPITALS RESEARCH DEVELOPMENT INC,
WEITZ Jeffrey,
HIRSH Jack,
Inventor(s):
WEITZ Jeffrey,
HIRSH Jack,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9855515 A1 **19981210**
Application: WO 98CA548 19980605 (PCT/WO CA9800548)
Priority Application: US 9772098 19970606
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: C08B-037/10
International Patent Class: A61K-31:725
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 11949

English Abstract
The present invention provides compositions and methods for the treatment of cardiovascular diseases. More particularly, the present invention relates to modifying thrombus formation by administering an agent which, inter alia, is capable of (**1**) inactivating fluid-phase **thrombin** and **thrombin** which is bound either to fibrin in a clot or to some other surface by catalyzing antithrombin; and (2) inhibiting thrombin generation by catalyzing factor Xa inactivation by antithrombin III (ATIII). The compositions and methods of the present invention are particularly useful for preventing thrombosis in the circuit of cardiac bypass apparatus and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from thrombus-related cardiovascular conditions, such as unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc.

French Abstract
L'invention concerne des compositions et des methodes permettant de traiter les maladies cardio-vasculaires. Plus particulierement, elle permet de modifier la formation du thrombus grace a l'administration d'un agent qui, entre autres, est capable de: (**1**) inactiver la **thrombine** en phase fluide et la **thrombine** liee soit a la fibrine contenue dans un caillot, soit a une autre surface, en catalysant l'antithrombine; et (2) inhiber la production de thrombine en catalysant l'inactivation du facteur Xa par l'antithrombine III (AT III). Les compositions et les methodes de la presente invention sont particulierement utiles pour prevenir les thromboses dans le circuit d'un appareil de circulation extra-corporelle et chez les patients dialyses, ainsi que pour traiter les patients souffrant de ou susceptibles de souffrir de troubles cardio-vasculaires lies a un thrombus, tels qu'angor instable, infarctus du myocarde, accident vasculaire cerebral (attaque), embolie pulmonaire, thrombose des veines profondes, thrombose arterielle, etc.

24/5/41 (Item 5 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

00464714 **Image available**
PERFUSION BALLOON AND RADIOACTIVE WIRE DELIVERY SYSTEM
BALLONNET DE PERFUSION ET DISPOSITIF D'ADMINISTRATION A FIL RADIOACTIF
Patent Applicant/Assignee:
SCIMED LIFE SYSTEMS INC,
Inventor(s):
HASTINGS Roger N,
URICK Michael J,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9855179 A1 **19981210**
Application: WO 98US10235 19980519 (PCT/WO US9810235)
Priority Application: US 97482 19970603
Designated States: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61N-005/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 10450
English Abstract
This invention is a **catheter** (320) capable of irradiating blood vessel walls to inhibit restenosis after angioplasty. **Catheters** (320) are capable of simultaneous irradiation, angioplasty, and in some devices **drug infusion** . Preferred **catheters** (320) include a helical **perfusion** balloon (336) having strand windings (346) spaced apart when inflated, and defining a perfusion **lumen** (356) within. A tubular sheath (374) over the helical strands (346), and distal shaft region (326) is used in some embodiments and defines an outer wall for the perfusion **lumen** (356). A spiral, inter-strand space (376) is defined between the sheath outer wall, and the blood vessel inner wall providing a confined volume for controlled **delivery** of **drugs** to the vessel wall in conjunction with irradiation. A device having a radiation wire distally closed end tube is provided. A device having a radiation wire open ended tube terminating proximally of the perfusion **lumen** is also provided.

French Abstract
L'invention concerne un **catheter** (320) pouvant irradier les parois du vaisseau sanguin pour inhiber une restenose apres une angioplastie. Les **catheters** (320) de l'invention peuvent a la fois effectuer une irradiation, une angioplastie et, dans certains dispositifs, une infusion de medicaments. Des **catheters** preferes (320) incluent un ballonnet de perfusion (336) muni d'enroulements de fils (346) espaces lorsque le ballonnet est gonfle et delimitant une lumiere de perfusion (356) placee a l'interieur. Une gaine tubulaire (374) recouvrant les fils spirales (346) et une partie de manchon distale (326) est utilisee dans certaines formes de realisation et delimite une paroi externe pour la lumiere de perfusion (356). Un espace spirale (376) entre les fils est delimite entre la paroi externe de la gaine et la paroi interne du vaisseau sanguin et presente un volume captif pour combiner un apport regule de medicaments a la paroi vasculaire et une irradiation. L'invention concerne en outre un dispositif comprenant un tube terminal a fil radioactif et fermeture distale; elle concerne enfin un dispositif comprenant un tube extensible a fil radioactif arrivant a proximite de la lumiere de perfusion.

24/5/42 (Item 6 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00464677
METHODS FOR TREATING THROMBOTIC DISORDERS
PROCEDE DE TRAITEMENT DE TROUBLES THROMBOTIQUES
Patent Applicant/Assignee:

ELI LILLY AND COMPANY,
GRINNELL Brian William,
JAKUBOWSKI Joseph Anthony,
Inventor(s):
GRINNELL Brian William,
JAKUBOWSKI Joseph Anthony,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9855142 A1 **19981210**
Application: WO 98US11071 19980601 (PCT/WO US9811071)
Priority Application: US 9748628 19970605
Designated States: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: A61K-038/48
International Patent Class: A01N-37:36
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5110

English Abstract
The present invention provides a method of treatment for patients with a variety of thrombotic disorders including, but not limited to, stroke, venous thrombosis, myocardial infarction, unstable angina, abrupt closure following angioplasty or stent placement, and thrombosis as a result of peripheral vascular surgery. Said treatment is a combination therapy with human aPC and antiplatelet agents including, but not limited to, aspirin (ASA), clopidogrel, ReoPro (abciximab), dipyridamole, ticlopidine and IIb/IIIa receptor antagonists. The synergy will result in the ability to reduce the dosages of the agents used in the combination therapy.

French Abstract
L'invention porte sur un procede de traitement de patients souffrant de differents troubles thrombotiques dont, non limitativement, les attaques, les thromboses veineuses, les infarctus du myocarde, l'angor instable, les obturations soudaines suivant une angioplastie ou la mise en place d'une prothese endovasculaire, ou une thrombose consecutive a une operation sur le systeme vasculaire peripherique. Ledit traitement est une therapie combinee d'aPC et d'antiplaquetaires dont, non limitativement: l'aspirine, le clopidogrel, le ReoPro (abciximab), la ticlopidine et les antagonistes des recepteurs IIb/IIIa. Cette synergie permet de reduire les dosages des differents agents utilises dans la therapie combinee.

24/5/65 (Item 29 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00422518 **Image available**
METHOD OF TREATING A DISEASE PROCESS IN A LUMINAL STRUCTURE
PROCEDE POUR TRAITER UN PROCESSUS PATHOLOGIQUE DANS UNE STRUCTURE LUMINALE
Patent Applicant/Assignee:
THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK,
WEINBERGER Judah Z,
Inventor(s):
WEINBERGER Judah Z,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9812979 A1 **19980402**
Application: WO 97US17286 19970925 (PCT/WO US9717286)
Priority Application: US 96721696 19960926
Designated States: AU CA JP MX US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61B-019/00
Publication Language: English

Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 20552
English Abstract
An apparatus and a method of inhibiting a disease process in a luminal structure of a subject comprising introducing within the luminal structure a complex of a radionuclide and a chelating agent in an amount effective to inhibit the disease process.

French Abstract
Cette invention se rapporte a un appareil et a un procede qui servent a inhiber un processus pathologique dans une structure luminale d'un sujet, ce procede consistant a introduire dans la structure luminale un complexe d'un radionucleide et d'un agent de chelation en quantite propre a inhiber le processus pathologique.

24/5/75 (Item 39 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00397987
RADIOACTIVITY LOCAL DELIVERY SYSTEM
SYSTEME DE RADIOTHERAPIE LOCALE
Patent Applicant/Assignee:
BERTRAND Olivier,
MONGRAIN Rosaire,
TANGUAY Jean-Francois,
BILODEAU Luc,
Inventor(s):
BERTRAND Olivier,
MONGRAIN Rosaire,
TANGUAY Jean-Francois,
BILODEAU Luc,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9738730 A2 **19971023**
Application: WO 97CA262 19970417 (PCT/WO CA9700262)
Priority Application: US 9615788 19960417
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: A61K-051/12
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 9845

English Abstract
The invention provides a radioactivity local delivery system enabling the use of isotopes having a longer half life and having a lower energy. The invention also provides a radioactivity local delivery system enabling an easier and more efficient control of the dose/rate and total dose of local radiation **delivery** . The present invention utilizes a **radioisotope** coupled to a circulation time reducing agent such as a chelatin agent, the coupled radioisotope being in releasable association with the structure to be inserted in a vessel of a human patient. The coupled radioisotope can be part of the support itself or in releasable association therewith through the use of a biodegradable or non-biodegradable pharmaceutical carrier. Also provided is a method to decrease the growth of actively proliferating cells at a targeted site in a vessel of a human patient as well as compositions therefor.

French Abstract
La presente invention concerne un systeme de radiotherapie locale

permettant d'utiliser des isotopes ayant une demi-vie plus longue et une energie moindre. L'invention concerne egalement un systeme de radiotherapie locale permettant de regler plus facilement et plus efficacement la dose/le taux et la dose totale du rayonement local. Dans la presente invention, on utilise un radio-isotope couple a un agent reduisant le temps de circulation tel qu'un agent chelateur, le radio-isotope couple etant associe a la structure a inserer dans le vaisseau d'un patient humain de maniere a pouvoir en etre libere. Le radio-isotope couple peut faire partie du support lui-meme ou lui etre associe au moyen d'un excipient pharmaceutique biodegradable ou non biodegradable dont il peut se liberer. On decrit egalement un procede et des compositions permettant de reduire la croissance des cellules proliferatives en un site cible d'un vaisseau d'un patient humain.

24/5/87 (Item 51 from file: 349)

00385267

ANTICOAGULANT AGENTS USEFUL IN TREATMENT OF THROMBOSIS
AGENTS COAGULANTS UTILES DANS LE TRAITEMENT DE LA THROMBOSE

Patent Applicant/Assignee:
SMITHKLINE BEECHAM CORPORATION,
UNIVERSITY OF VERMONT AND STATE AGRICULTURAL COLLEGE,
BLACKBURN Michael Neal,
CHURCH William Robert,
FEUERSTEIN Giora Zeev,
GROSS Mitchell Stuart,
NICHOLS Andrew John,
PADLAN Eduardo Agustin,
PATEL Arunbhai Haribhai,
SYLVESTER Daniel Robert,
Inventor(s):
BLACKBURN Michael Neal,
CHURCH William Robert,
FEUERSTEIN Giora Zeev,
GROSS Mitchell Stuart,
NICHOLS Andrew John,
PADLAN Eduardo Agustin,
PATEL Arunbhai Haribhai,
SYLVESTER Daniel Robert,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9726010 A1 **19970724**
Application: WO 97US759 19970117 (PCT/WO US9700759)
Priority Application: US 9610108 19960117; US 9629119 19961024
Designated States: AL AM AU BB BG BR CA CN CZ EE GE HU IL IS JP KG KP KR LK LR LT LV MD MG MK MN MX NO NZ PL RO SG SI SK TR TT UA US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: A61K-039/395
International Patent Class: C12N-05:12
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 32196

English Abstract
Monoclonal antibodies directed against coagulation factors and their use in inhibiting thrombosis are disclosed.
French Abstract
L'invention se rapporte a des anticorps monoclonaux diriges contre des facteurs de coagulation et a leur utilisation dans l'inhibition de la thrombose.

24/5/90 (Item 54 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

00382137
USE OF RC-9 IN DIAGNOSIS AND TREATMENT OF PROLIFERATIVE ARTERIAL DISEASE
UTILISATION DU GENE RC-9 POUR LE DIAGNOSTIC ET LE TRAITEMENT DES MALADIES ARTERIELLES PROLIFERATIVES
Patent Applicant/Assignee:
SMITHKLINE BEECHAM CORPORATION,
OHLSTEIN Eliot Howard,
ARLETH Anthony Joseph,
AUTIERI Michael Victor,
Inventor(s):
OHLSTEIN Eliot Howard,
ARLETH Anthony Joseph,
AUTIERI Michael Victor,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9722880 A1 **19970626**
Application: WO 96US19671 19961213 *(PCT/WO US9619671)*
Priority Application: US 958801 19951218
Designated States: AL AM AU BB BG BR CA CN CZ EE GE HU IL IS JP KG KP KR LK LR LT LV MD MG MK MN MX NO NZ PL RO SG SI SK TR TT UA US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: G01N-033/563
International Patent Class: G01N-33:559; G01N-33:537; G01N-33:531; G01N-33:53; G01N-33:542; C12Q-01:68
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 9912

English Abstract
The present invention provides methods of using the polynucleotide sequences, recombinant RC-9 proteins encoded thereby, and RC-9 antibodies in diagnosis and treatment of atherosclerosis.

French Abstract
On decrit des procedes d'utilisation de sequences polynucleotides, des proteines de RC-9 recombinees codees par ces sequences, et des anticorps de RC-9 servant au diagnostic et au traitement de l'atherosclerose.

24/5/94 (Item 58 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00376356 **Image available**
BALLOON CATHETER **FOR DRUG APPLICATION**
CATHETER **A BALLONNET POUR L'APPLICATION DE MEDICAMENTS**
Patent Applicant/Assignee:
C R BARD INC,
Inventor(s):
ENGER Christine D,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9717099 A1 **19970515**
Application: WO 96US17434 19961029 (PCT/WO US9617434)
Priority Application: US 95553973 19951106
Designated States: JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-025/10
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5738

English Abstract

A method, and an apparatus for use in practicing the method, are provided by which a highly concentrated medication or chemotherapeutic agent can be applied locally under sufficient pressure to cause the medication or agent to penetrate into localized tissue or a body **lumen** . The total volume of medication or agent is quite small, well below levels that might cause an adverse reaction in other parts of the body. The **catheter** includes a thin wall flexible balloon having two collars and a central region between the collars, when the central regions defines a plurality of regularly spaced minute perforations through which medication may weep at a controlled, low **flow rate** . The **flow rate** is controlled by the minute perforations and the diameter of the central region is less than the diameter of the collars. In practicing the method of the invention, the balloon is selected such that the inflated diameter of the collars will correspond to or be slightly greater than the diameter of **lumen** into which the balloon is placed, and the central region will be slightly less than that **lumen** diameter, thereby defining a distinct, annular medication reservoir between the balloon and body **lumen** . The depth of the reservoir reduces the risk of medicine jetting against the vessel **lumen** if excess pressure is applied. Inflation of the balloon with a medication will cause the medication to weep from the central region of the balloon, consequently filling the reservoir and bathing the **lumen** walls. After a predetermined time, a sufficient amount of medication will be absorbed by the **lumen** walls and the balloon will be deflated so that the **catheter** may be withdrawn from the **lumen** . The quantity of medication that ultimately flows into the vessel **lumen** is sufficiently small so as to not cause any other systemic damage to the patient.

French Abstract

L'invention porte sur un procede et l'appareil associe au moyen desquels un medicament fortement concentre ou un agent chimiotherapeutique peuvent etre appliques localement sous une pression suffisamment elevee pour leur permettre de penetrer dans un tissu cible ou un orifice corporel. Le volume total de medicament ou d'agent est tres faible et notablement inferieur aux doses susceptibles de provoquer une reaction adverse dans d'autres parties du corps. Le **catheter** comporte un ballonnet souple a paroi mince comportant deux colliers et une zone centrale situee entre les colliers et percee d'une serie de perforations minuscules regulierement espaces par lesquels le medicament peut suinter avec un debit donne tres faible. La regulation du debit resulte de la taille des perforations, le diametre de la region centrale etant inferieur a celui des colliers. Le ballonnet est choisi de maniere a ce que le diametre des colliers une fois gonfles soit egal ou legerement superieur a celui de la lumiere ou l'on place le ballonnet, et que celui de la zone centrale lui soit legerement inferieur. On constitue ainsi un reservoir annulaire separe de medicament entre le ballonnet et le corps de la lumiere. L'epaisseur du reservoir reduit le risque de projection du medicament contre la lumiere du vaisseau en cas de pression trop forte. Lorsqu'on gonfle le ballonnet a l'aide d'un medicament, ce dernier suinte de la zone centrale du ballonnet, remplit le reservoir et baigne les parois de la lumiere. Apres un temps donne, les parois de la lumiere ayant absorbe une quantite suffisante de medicament, on degonfle le ballonnet pour pouvoir extraire le **catheter** de la lumiere. La quantite de medicament passant finalement dans la lumiere du vaisseau est suffisamment faible pour ne causer aucun autre dommage systemique au patient.

24/5/113 (Item 77 from file: 349)

00349632 **Image available**

SELECTIVE AORTIC PERFUSION SYSTEM
SYSTEME DE PERFUSION AORTIQUE SELECTIF

Patent Applicant/Assignee:
NEW YORK UNIVERSITY,
Inventor(s):
PARADIS Norman A,

Patent and Priority Information (Country, Number, Date):
  Patent: WO 9632145 A1 **19961017**
  Application: WO 95US4531 19950411 (PCT/WO US9504531)
  Priority Application: WO 95US4531 19950411
Designated States: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-001/10
International Patent Class: A61B-17:12
Publication Language: English
Fulltext Availability:
  Detailed Description
  Claims
Fulltext Word Count: 8002

English Abstract
An apparatus for improving cardiopulmonary resuscitation involves use of a **catheter** having both an occlusion balloon and a pumping balloon. The occlusion balloon occludes the aorta such that all pumping action will be restricted to the blood vessels above the balloon occlusion. The pumping balloon is cephalad to the occlusion balloon and is preferably pumped in synchronization with external cardiocirculatory resuscitation. The pumping balloon preferably inflates first at the caudal end and then sequentially to the cephalad end in order to provide unidirectional cephalad pumping. Oxygen-carrying fluid may be infused through the **lumen** into the aorta cephalad of the pumping balloon during use.

French Abstract
Appareil concu pour ameliorer la reanimation cardio-respiratoire, qui implique l'utilisation d'un **catheter** pourvu d'un ballonnet d'occlusion et d'un ballonnet de contre-pulsation. Le ballonnet d'occlusion bouche l'aorte de sorte que la totalite de l'action de pompage soit limitee aux vaisseaux sanguins situes au-dessus de l'occlusion. Le ballonnet de contre-pulsation est place en direction cephalique par rapport au ballonnet d'occlusion et est de preference actionne en synchronisation avec la reanimation cardio-respiratoire externe. Le ballonnet de contre-pulsation se gonfle de preference d'abord au niveau de l'extremite caudale, puis progressivement vers l'extremite cephalique, en vue de produire une contre-pulsation unidirectionnelle en direction cephalique. Le fluide porteur d'oxygene peut etre perfuse par le **lumen** pour etre introduit dans l'aorte du cote cephalique par rapport au ballonnet de contre-pulsation utilise lors de cette reanimation.

24/5/114 (Item 78 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00347551 **Image available**
MULTIPLE HOLE DRUG DELIVERY **BALLOON**
BALLONNET D'ADMINISTRATION DE MEDICAMENTS A ORIFICES MULTIPLES
Patent Applicant/Assignee:
  BOSTON SCIENTIFIC CORPORATION,
Inventor(s):
  ROPIAK Susan M,
Patent and Priority Information (Country, Number, Date):
  Patent: WO 9630064 A1 **19961003**
  Application: WO 96US4361 19960329 (PCT/WO US9604361)
  Priority Application: US 95414650 19950331
Designated States: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-005/00
International Patent Class: A61M-25:00; A61M-29:00
Publication Language: English
Fulltext Availability:
  Detailed Description
  Claims
Fulltext Word Count: 5033

English Abstract
An inflatable medical device (10) for delivery of medication to an organ

24/5/114 (Item 78 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00347551 **Image available**
MULTIPLE HOLE DRUG DELIVERY **BALLOON**
BALLONNET D'ADMINISTRATION DE MEDICAMENTS A ORIFICES MULTIPLES
Patent Applicant/Assignee:
BOSTON SCIENTIFIC CORPORATION,
Inventor(s):
ROPIAK Susan M,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9630064 A1 **19961003**
Application: WO 96US4361 19960329 (PCT/WO US9604361)
Priority Application: US 95414650 19950331
Designated States: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-005/00
International Patent Class: A61M-25:00; A61M-29:00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5033

English Abstract
An inflatable medical device (10) for delivery of medication to an organ in the body having a multi- **lumen** **catheter** (12) and a hollow, inflatable channel-like medication deliverable balloon (14) at the distal end of the **catheter** . A plurality of conduits (32) extend along the balloon between the walls (42, 44) of the balloon for delivery of medications. Each conduit includes an array (40) of closely spaced apertures for allowing medications in the conduits to transfer out of the conduits into a surrounding vessel after the balloon is inflated.

French Abstract
Instrument medical (10) gonflable destine a administrer des medicaments a un organe du corps, pourvu d'un **catheter** (12) a plusieurs lumieres et d'un ballonnet (14) d'administration de medicaments en forme de canal, creux, gonflable et situe a l'extremite distale du **catheter** . Une pluralite de conduits (32) s'etendent le long du ballonnet entre les parois (42, 44) de celui-ci afin d'administrer des medicaments. Chaque conduit comporte un ensemble (40) d'ouvertures faiblement espacees les unes des autres afin de permettre aux medicaments se trouvant dans les conduits de se transferer de ces derniers a un recipient les entourant apres le gonflage du ballonnet.

24/5/131 (Item 95 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00308621
PERFUSION SHUNT DEVICE FOR RECEIVING ANGIOPLASTY BALLOON
DISPOSITIF DE DERIVATION DE PERFUSION POUR RECEVOIR UN BALLONNET D'ANGIOPLASTIE
Patent Applicant/Assignee:
LOCALMED INC,
Inventor(s):
KLEIN Enrique J,
BAJOR Jordan,
ALBA Paul,
KAPLAN Aaron V,
GOELD Paul K,
EVARD Philip C,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9526773 A1 **19951012**
Application: WO 95US4191 19950403 (PCT/WO US9504191)

Priority Application: US 94221613 19940401; US 94305250 19940913; US 95401541 19950310
Designated States: AU CA JP KR NZ AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-025/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 11444

English Abstract
A perfusion shunt device (10) is used in conjunction with balloon **catheters** to provide blood perfusion across an inflated balloon in a blood vessel. The perfusion shunt device (10) comprises a flexible conduit structure (12) having one or more blood perfusion paths (24) formed from a proximal end to a distal end thereof. The flexible conduit structure (12) is usually attached directly or indirectly to a proximal shaft structure. Discrete anchors or expansible sleeves or cages are provided for locating the conduit structure (12) over the balloon on the **catheter** . The device may be loaded over a conventional angioplasty balloon **catheter** outside of the blood vessel being treated, either before or after an angioplasty procedure. In an alternative embodiment, a non-distensible pouch (312) is formed integrally with the flexible conduit structure (12) in order to receive the balloon of a balloon angioplasty **catheter** . The non-distensible nature of the pouch limits the inflated balloon size.

French Abstract
Dispositif de derivation de perfusion (10) utilise en association avec des sondes a ballonnet pour permettre une perfusion sanguine autour d'un ballonnet gonfle dans un vaisseau sanguin. Ledit dispositif de derivation de perfusion (10) comprend un conduit flexible (12) muni d'un ou de plusieurs canaux de perfusion sanguine (24) allant d'une extremite proximale a une extremite distale du conduit. Ce conduit flexible (12) est generalement fixe directement ou indirectement a un axe proximal. Des elements d'ancrage discrets ou des manchons ou cages expansibles sont prevus pour placer le conduit (12) sur le ballonnet de la sonde. Ce dispositif peut etre place sur une sonde a ballonnet pour angioplastie classique a l'exterieur du vaisseau sanguin en cours de traitement, soit avant soit apres une angioplastie. Dans un autre mode de realisation, une poche non dilatable (312) fait partie integrante du conduit flexible (12) afin de recevoir le ballonnet d'une sonde pour angioplastie a ballonnet. La nature non dilatable de la poche permet de limiter la taille du ballonnet gonfle.

24/5/146 (Item 110 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00273144 **Image available**
FLUID DELIVERY CATHETER
CATHETER **D'ADMINISTRATION DE LIQUIDES**
Patent Applicant/Assignee:
ADVANCED CARDIOVASCULAR SYSTEMS INC,
Inventor(s):
MACHOLD Timothy R,
ROBINSON Janine C,
MICHAELS Mary Beth,
SIRHAN Motasim M,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9421320 A1 **19940929**
Application: WO 94US2701 19940314 (PCT/WO US9402701)
Priority Application: US 93569 19930315
Designated States: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-029/02
Publication Language: English

Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 6265

English Abstract
A **catheter** and method of using the **catheter** for the delivery of therapeutic or diagnostic liquid within a body **lumen** of a patient. The **catheter** (10) has an outer inflatable member (19) which has a wall with a plurality of apertures (20) which eject therapeutic or diagnostic liquid in a jet-like form deep within the **lumenal** tissue adjacent to the outer inflatable member (19). In one embodiment the **catheter** has an inner inflatable member (16) disposed within the outer inflatable member (19) which upon inflation expands the outer tubular member (19) so as to dilatate a stenotic region of a body **lumen** such as an artery. The inflatable member may be provided with proximal and distal ends which expand to larger diameters than the central inflatable section so as to seal the larger ends and prevent the loss of fluid.

French Abstract
Catheter et procede d'utilisation dudit **catheter** pour l'administration de liquide therapeutique ou diagnostique dans une lumiere du corps d'un patient. Ledit **catheter** (10) possede un element gonflable externe (19) dote d'une paroi presentant une pluralite d'ouvertures (20) qui ejectent du liquide therapeutique ou diagnostique sous forme de jet profondement au sein du tissu de la lumiere adjacent a l'element gonflable externe (19). Dans un mode de realisation, le **catheter** possede un element gonflable interne (16) place a l'interieur de l'element gonflable externe (19), qui, lors du gonflage, dilate l'element tubulaire externe (19) de maniere a dilater une region stenosee d'une lumiere du corps, telle qu'une artere. L'element gonflable peut etre dote d'extremites proximale et distale qui se dilatent pour atteindre des diametres plus importants que la partie gonflable centrale, de maniere a bloquer hermetiquement les extremites plus larges et a empecher la perte de liquide.
?

28/5/1 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00807164
MULTIPLE HOLE DRUG DELIVERY BALLOON
BALLONKATHETER MIT MEHREREN LOCHERN ZUR ARZNEIMITTELABGABE
BALLONNET D'ADMINISTRATION DE MEDICAMENTS A ORIFICES MULTIPLES
PATENT ASSIGNEE:
BOSTON SCIENTIFIC CORPORATION, (1064392), One Boston Scientific Place, Natick, MA 01760-1537, (US), (Proprietor designated states: all)
INVENTOR:
ROPIAK, Susan, M., 36 Patterson Road, Hanscom Air Force Base, MA 01731, (US)
LEGAL REPRESENTATIVE:
Warren, Anthony Robert et al (37331), BARON & WARREN, 18 South End, Kensington, London W8 5BU, (GB)
PATENT (CC, No, Kind, Date): EP 819011 A1 980121 (Basic)
EP 819011 A1 990804
EP 819011 B1 030312
WO 96030064 961003
APPLICATION (CC, No, Date): EP 96910669 960329; WO 96US4361 960329
PRIORITY (CC, No, Date): US 414650 950331
DESIGNATED STATES: DE; FR; GB; IE
INTERNATIONAL PATENT CLASS: A61M-005/00; A61M-025/00; A61M-029/00
CITED PATENTS (EP B): EP 383429 A; US 4994033 A; US 5254089 A; US 5514092 A
NOTE:
No A-document published by EPO
LEGAL STATUS (Type, Pub Date, Kind, Text):

Examination:	010926 A1	Date of dispatch of the first examination report: 20010810
Application:	961218 A	International application (Art. 158(1))
Grant:	030312 B1	Granted patent
Application:	980121 A1	Published application (A1with Search Report ;A2without Search Report)
Examination:	980121 A1	Date of filing of request for examination: 971027
Search Report:	990804 A1	Drawing up of a supplementary European search report: 990617

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200311	526
CLAIMS B	(German)	200311	591
CLAIMS B	(French)	200311	586
SPEC B	(English)	200311	3856
Total word count - document A			0
Total word count - document B			5559
Total word count - documents A + B			5559

28/5/4 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00712573
Coaxial/Double lumen catheter.
Koaxial doppellumiger Katheter.
Catheter a double passage coaxial.
PATENT ASSIGNEE:
LEOCOR, INC., (1088753), 1301 Regent's Park Drive, Houston, Texas 77058, (US), (applicant designated states: BE;DE;FR;GB;IT;LU;NL)
INVENTOR:
Wijay, Bandula, 1301 Regent's Park Drive, Houston, Texas 77058, (US)
LEGAL REPRESENTATIVE:
Le Vrang, Klaus (44745), Fliederstrasse 1, D-85139 Wettstetten, (DE)
PATENT (CC, No, Kind, Date): EP 674912 A1 951004 (Basic)
APPLICATION (CC, No, Date): EP 95101378 950202;

PRIORITY (CC, No, Date): US 221363 940331
DESIGNATED STATES: BE; DE; FR; GB; IT; LU; NL
INTERNATIONAL PATENT CLASS: A61M-029/02;

ABSTRACT EP 674912 A1
The present invention provides a low-profile **balloon** catheter which is extremely maneuverable and capable of dilating an **occluded artery** with minimal risk of angina. The catheter is highly maneuverable because its distal section has substantially coaxial inner and outer tubes which are in relatively tight mechanical communication at their proximal end and their distal ends are mechanically connected only via the **balloon** . As a result, the inner distal tube is relatively independent of the outer distal tube. The proximal section of the catheter is relatively stiff and preferably has two lumens therethrough. One lumen, which is substantially larger, is used to actively **perfuse** oxygenated blood, **drugs** , or dyes distal to the tip of the **catheter** at **flowrates** up to about 100 **cc** /min. Preferably, the inner surface of this first perfusion **lumen** has a shape at its inner surface that permits the second, smaller lumen to "nest" adjacent to and substantially within said inner surface of said first perfusion lumen. This "nesting" relationship between the two lumens maximizes the area of the proximal section that can be used for perfusion and insertion of the guidewire and **inflation** fluid through the second lumen. In order to provide a flexible, more maneuverable distal tip for the catheter, the first perfusion lumen is in fluid communication with an inner, substantially coaxial tube in the distal section of the catheter. This inner tube extends through an outer tube that is mechanically connected to the catheter and to the proximal end of the **balloon** . The inner tube extends through the **balloon** , which is mechanically connected to the inner tube at its distal end, and then empties the contents from the first perfusion lumen at the distal end of the catheter. (see image in original document)
ABSTRACT WORD COUNT: 291

LEGAL STATUS (Type, Pub Date, Kind, Text):
Application: 951004 A1 Published application (A1with Search Report ;A2without Search Report)
Withdrawal: 970108 A1 Date on which the European patent application was deemed to be withdrawn: 960404
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	288
SPEC A	(English)	EPAB95	3163
Total word count - document A			3451
Total word count - document B			0
Total word count - documents A + B			3451

28/5/5 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00620266
CATHETER WITH ATRAUMATIC DRUG DELIVERY **TIP**
KATHETER MIT ATRAUMATISCHER SPITZE ZUR VERABREICHUNG VON ARZNEIEN
CATHETER A POINTE DE LIBERATION ATRAUMATIQUE DE MEDICAMENT
PATENT ASSIGNEE:
TARGET THERAPEUTICS, INC., (1310821), 47900 Bayside Parkway, Fremont, CA 94538, (US), (Proprietor designated states: all)
INVENTOR:
CHEE, U., Hiram, 127 Dolton Avenue, San Carlos, CA 94030, (US)
LEMOURE, Edward, R., 67 Howard Avenue, New Haven, CT 06519, (US)
LEGAL REPRESENTATIVE:
Price, Nigel John King (62102), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 618819 A1 941012 (Basic)
EP 618819 A1 950426
EP 618819 B1 991201

WO 9407549 940414
APPLICATION (CC, No, Date): EP 93921670 930917; WO 93US8834 930917
PRIORITY (CC, No, Date): US 954669 920930
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61M-025/00
CITED PATENTS (EP B): EP 476796 A; DE 3314755 A; GB 2182567 A; US 4149535 A ; US 4173981 A; US 4391276 A; US 4808158 A; US 4842590 A; US 4848344 A; US 5158084 A
NOTE:
No A-document published by EPO
LEGAL STATUS (Type, Pub Date, Kind, Text):

Lapse:	001025 B1	Date of lapse of European Patent in a contracting state (Country, date): BE 19991201, PT 20000302,
Application:	940720 A	International application (Art. 158(1))
Lapse:	020626 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19991201, BE 19991201, CH 19991201, LI 19991201, ES 19991201, PT 20000302, SE 19991201,
Lapse:	001227 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19991201, BE 19991201, CH 19991201, LI 19991201, PT 20000302,
Lapse:	001213 B1	Date of lapse of European Patent in a contracting state (Country, date): BE 19991201, CH 20000307, LI 20000307, PT 20000302,
Oppn None:	001115 B1	No opposition filed: 20000902
Lapse:	001220 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19991201, BE 19991201, CH 20000307, LI 20000307, PT 20000302,
Lapse:	020605 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19991201, BE 19991201, CH 19991201, LI 19991201, PT 20000302, SE 19991201,
Application:	941012 A1	Published application (Alwith Search Report ;A2without Search Report)
Examination:	941012 A1	Date of filing of request for examination: 940411
Change:	950315 A1	International patent classification (change)
Search Report:	950426 A1	Drawing up of a supplementary European search report: 950315
Examination:	970416 A1	Date of despatch of first examination report: 970225
*Assignee:	990707 A1	Applicant (name, address) (change)
Grant:	991201 B1	Granted patent

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9948	792
CLAIMS B	(German)	9948	780
CLAIMS B	(French)	9948	872
SPEC B	(English)	9948	2566
Total word count - document A			0
Total word count - document B			5010
Total word count - documents A + B			5010

28/5/6 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00594590
Catheter for dilating stenotic lesions
Katheter zur Dilatation von stenosischen Schaden

Catheter pour dilater des lesions stenotiques
PATENT ASSIGNEE:
SciMed Life Systems, Inc., (952164), 8200 SciMed Place, Maple Grove, Minnesota 55311, (US), (Proprietor designated states: all)
INVENTOR:
Wijai, Bandula, 1903 Carriage Creek, Friendswood TX 77456, (US)
Angelini, Paolo, 1568 Kirby Drive, Houston TX 77099, (US)
LEGAL REPRESENTATIVE:
Winter, Brandl, Furniss, Hubner, Ross, Kaiser, Polte, Kindermann Partnerschaft (100053), Patent- und Rechtsanwaltskanzlei Patentanwalte, Rechtsanwalt Alois-Steinecker-Strasse 22, 85354 Freising, (DE)
PATENT (CC, No, Kind, Date): EP 597465 A1 940518 (Basic)
EP 597465 B1 000209
APPLICATION (CC, No, Date): EP 93118227 880920;
PRIORITY (CC, No, Date): US 100363 870923
DESIGNATED STATES: DE; FR; GB
RELATED PARENT NUMBER(S) - PN (AN):
EP 383794 (EP 88909045)
INTERNATIONAL PATENT CLASS: A61M-029/02
CITED PATENTS (EP B): EP 260711 A; WO 87/00442 A; GB 156674 A; GB 2172205 A ; US 3924634 A; US 4692148 A

ABSTRACT EP 597465 A1
A catheter for dilating stenotic lesions has an elongated body (I) with at least one lumen (12) extending therethrough. A tip (T), constructed of materials softer than the elongated body is attached to the distal end of the body. The tip segment has at least one lumen (14) passing therethrough which is in alignment with the lumen (12) in the elongated body. A guide is adapted to pass through the aligned lumens. A **balloon** (D) is connected to the distal segment of the elongated body over its outer periphery, thereby creating a **balloon** cavity (24) therebetween. At least one additional lumen (A) is provided in the elongated body in flow communication with the **balloon** cavity, for selective **inflation** and deflation thereof, with a contrast fluid.
ABSTRACT WORD COUNT: 127
NOTE:
Figure number on first page: NONE

LEGAL STATUS (Type, Pub Date, Kind, Text):

Oppn None:	010124 B1	No opposition filed: 20001110
Grant:	20000209 B1	Granted patent
Application:	940518 A1	Published application (A1with Search Report ;A2without Search Report)
Examination:	940518 A1	Date of filing of request for examination: 931125
Examination:	951102 A1	Date of despatch of first examination report: 950913

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200006	785
CLAIMS B	(German)	200006	793
CLAIMS B	(French)	200006	856
SPEC B	(English)	200006	7229
Total word count - document A			0
Total word count - document B			9663
Total word count - documents A + B			9663

28/5/8 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00585492
SELECTIVE AORTIC PERFUSION SYSTEM
SELEKTIVES AORTAPERFUSIONSYSTEM
SYSTEME DE PERFUSION AORTIQUE SELECTIVE
PATENT ASSIGNEE:

NEW YORK UNIVERSITY, (300275), 550 First Avenue, Room MSB 153, New York, NY 10016, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;MC;NL;SE)

INVENTOR:
PARADIS, Norman, A., 48 Remsen Street, Brooklyn, NY 11201, (US)

LEGAL REPRESENTATIVE:
Rau, Manfred, Dr. Dipl.-Ing. et al (38392), Rau, Schneck & Hubner Patentanwalte Konigstrasse 2, 90402 Nurnberg, (DE)

PATENT (CC, No, Kind, Date): EP 603308 A1 940629 (Basic)
EP 603308 A1 950628
EP 603308 B1 990721
WO 9304728 930318

APPLICATION (CC, No, Date): EP 92920154 920909; WO 92US7605 920909

PRIORITY (CC, No, Date): US 756693 910909

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; SE

INTERNATIONAL PATENT CLASS: A61M-029/00; A61M-025/00; A61B-017/12;

CITED PATENTS (WO A): US 4759976 A ; US 4554953 A ; US 5066532 A ; US 4759391 A ; US 5098522 A

NOTE:
No A-document published by EPO

LEGAL STATUS (Type, Pub Date, Kind, Text):

Lapse:	000607	B1	Date of lapse of European Patent in a contracting state (Country, date): DE 19991022,
Application:	940629	A1	Published application (A1with Search Report ;A2without Search Report)
Lapse:	030502	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, ES 19990721, GB 19991021, GR 19990721, IE 19990921, MC 20000331, NL 19990721, SE 19990721,
Lapse:	030212	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, ES 19990721, GB 19991021, GR 19990721, IE 19990921, MC 20000331, NL 19990721, SE 19990721,
Lapse:	020605	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, GB 19991021, GR 19990721, IE 19990921, MC 20000331, SE 19990721,
Lapse:	010321	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, GB 19991021, IE 19990921, MC 20000331,
Lapse:	001227	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, MC 20000331,
Oppn None:	000712	B1	No opposition filed: 20000426
Lapse:	000614	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, DE 19991022,
Lapse:	001213	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19991026, LI 19991026, DE 19991022,
Lapse:	010228	B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, GB 19991021, MC 20000331,
Lapse:	010606	B1	Date of lapse of European Patent in a

		contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, GB 19991021, GR 19990721, IE 19990921, MC 20000331,
Lapse:	020619 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, ES 19990721, GB 19991021, GR 19990721, IE 19990921, MC 20000331, SE 19990721,
Lapse:	030423 B1	Date of lapse of European Patent in a contracting state (Country, date): AT 19990721, BE 19990721, CH 19990721, LI 19990721, DE 19991022, ES 19990721, GB 19991021, GR 19990721, IE 19990921, MC 19990930, NL 19990721, SE 19990721,
Examination:	940629 A1	Date of filing of request for examination: 940322
Change:	950517 A1	Obligatory supplementary classification (change)
Search Report:	950628 A1	Drawing up of a supplementary European search report: 950510
Examination:	970521 A1	Date of despatch of first examination report: 970407
Grant:	990721 B1	Granted patent

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9929	778
CLAIMS B	(German)	9929	782
CLAIMS B	(French)	9929	926
SPEC B	(English)	9929	3890
Total word count - document A			0
Total word count - document B			6376
Total word count - documents A + B			6376

28/5/9 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00542319
Drug delivery **catheter**
Arzneimittelabgabekatheter
Catheter destine a l'application de medicaments
PATENT ASSIGNEE:
SCIMED LIFE SYSTEMS, INC., (952161), 6655 Wedgwood Road, Maple Grove, MN 55369-7503, (US), (applicant designated states: BE;DE;FR;GB;LU;NL)
INVENTOR:
Schweich, Cyril J., Jr., 2140 Eleanor Avenue, St. Paul, Minnesota 55116, (US)
Burns, Matthew M., 1180 Loma Linda Avenue, Orono, Minnesota 55364, (US)
Harrison, Kent D., 5651 69th Avenue North, No.305, Brooklyn Park, Minnesota 55429, (US)
LEGAL REPRESENTATIVE:
Baverstock, Michael George Douglas et al (28131), BOULT WADE TENNANT, 27 Furnival Street, London EC4A 1PQ, (GB)
PATENT (CC, No, Kind, Date): EP 526102 A1 930203 (Basic)
EP 526102 B1 980401
APPLICATION (CC, No, Date): EP 92306740 920723;
PRIORITY (CC, No, Date): US 740047 910802
DESIGNATED STATES: BE; DE; FR; GB; LU; NL
INTERNATIONAL PATENT CLASS: A61M-029/02;
CITED PATENTS (EP A): WO 8800071 A; US 4824436 A; WO 8911307 A; EP 399712 A

ABSTRACT EP 526102 A1
A **drug delivery** catheter with an **inflatable** blood flow lumen includes a flexible tubular shaft (30) and an **inflatable balloon**

assembly (10,12,14,16) disposed at the distal end of the shaft. The catheter is inserted into a vessel with the **balloon** assembly in an un-**inflated** form and the **balloon** member is positioned at the treatment site and **inflated** . The **balloon** member in an **inflated** form defines a region or pocket (26) between the **balloon** assembly and the vessel wall which contains the drug separate from blood flow. Apertures (40) are provided within the **balloon** assembly to provide the drug to the containment pocket. Blood is allowed to flow through the center (24) of the **inflated** **balloon** assembly. (see image in original document)
ABSTRACT WORD COUNT: 123

LEGAL STATUS (Type, Pub Date, Kind, Text):

Lapse:	20000216 B1	Date of lapse of European Patent in a contracting state (Country, date): BE 19980401, LU 19980731,
Application:	930203 A1	Published application (Alwith Search Report ;A2without Search Report)
Examination:	930929 A1	Date of filing of request for examination: 930802
Examination:	951018 A1	Date of despatch of first examination report: 950901
Grant:	980401 B1	Granted patent
Oppn None:	990324 B1	No opposition filed
Lapse:	990707 B1	Date of lapse of the European patent in a Contracting State: BE 980401

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9814	1166
CLAIMS B	(German)	9814	1054
CLAIMS B	(French)	9814	1211
SPEC B	(English)	9814	8707
Total word count - document A			0
Total word count - document B			12138
Total word count - documents A + B			12138

28/5/10 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00542081
Catheter with improved fluid infusion
Katheter mit Flussigkeitsinfusion
Catheter avec perfusion de liquide
PATENT ASSIGNEE:
DOW CORNING ENTERPRISES, (2219800), P.O. Box 994, Midland, Michigan 48686-0994, (US), (applicant designated states: DE;FR;GB;IT)
INVENTOR:
Fine, Michael Jay, 11839 NW 28th Street, Coral Springs, Florida, (US)
Rogers, Enora Susanne, 8120 NW 185th Terrace, Hialeah, Florida, (US)
LEGAL REPRESENTATIVE:
Hall, Marina et al (76001), Elkington and Fife Prospect House, 8 Pembroke Road, Sevenoaks, Kent TN13 1XR, (GB)
PATENT (CC, No, Kind, Date): EP 526042 A1 930203 (Basic)
EP 526042 B1 980513
APPLICATION (CC, No, Date): EP 92306486 920715;
PRIORITY (CC, No, Date): US 734381 910722
DESIGNATED STATES: DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61B-017/22;
CITED PATENTS (EP A): EP 315290 A; US 4917085 A; WO 8802243 A
ABSTRACT EP 526042 A1
According to the invention, there is provided an **intravascular** catheter (10) and **thrombectomy** procedure utilizing the catheter. The catheter comprises a flexible jacket (12) with a distal working head having a canalizing tip (24) rotatable at high speeds for removing thrombus from the lumen of a vessel A flexible drive assembly (26) extends through the jacket to rotate the tip and a plurality of infusion

ports (31) are formed adjacent the distal end of the jacket, capable of delivering a fluid contrast media at relatively high volumetric **flow rates** into the **lumen** of the vessel to locate the site of the thrombus. The canalizing tip is then rotated at high speed to homogenize and remove the thrombus from the lumen. (see image in original document)
ABSTRACT WORD COUNT: 127

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	930203	A1	Published application (A1with Search Report ;A2without Search Report)
Examination:	930609	A1	Date of filing of request for examination: 930401
Examination:	941026	A1	Date of despatch of first examination report: 940908
Change:	960228	A1	Representative (change)
*Assignee:	960228	A1	Applicant (transfer of rights) (change): Theratek International, Inc. (1889801) 14740 NW 60th Avenue Miami Lakes, Florida 33014 (US) (applicant designated states: DE;FR;GB;IT)
*Assignee:	960228	A1	Previous applicant in case of transfer of rights (change): DOW CORNING WRIGHT CORPORATION (742640) P.O. Box 100 5677 Airline Road Arlington Tennessee (US) (applicant designated states: DE;FR;GB;IT)
Change:	960403	A1	Representative (change)
Change:	970108	A1	Representative (change)
*Assignee:	970108	A1	Applicant (transfer of rights) (change): DOW CORNING ENTERPRISES (2219800) P.O. Box 994 Midland, Michigan 48686-0994 (US) (applicant designated states: DE;FR;GB;IT)
*Assignee:	970108	A1	Previous applicant in case of transfer of rights (change): Theratek International, Inc. (1889801) 14740 NW 60th Avenue Miami Lakes, Florida 33014 (US) (applicant designated states: DE;FR;GB;IT)
Grant:	980513	B1	Granted patent
Oppn None:	990506	B1	No opposition filed

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9820	353
CLAIMS B	(German)	9820	333
CLAIMS B	(French)	9820	391
SPEC B	(English)	9820	12564
Total word count - document A			0
Total word count - document B			13641
Total word count - documents A + B			13641

28/5/11 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00542077
Controller for intravascular catheter system
Steuerung fur intravaskulares Kathetersystem
Commande pour systeme de catheter intravasculaire
PATENT ASSIGNEE:
DOW CORNING WRIGHT CORPORATION, (742640), P.O. Box 100 5677 Airline Road, Arlington Tennessee, (US), (applicant designated states: DE;FR;GB;IT)
INVENTOR:
Sullivan, James Brian, 607 Midland Street, Pittsburgh, Pennsylvania, (US)
Moore, Eric Rex, 11318 Frankstown Road, Pittsburgh, Pennsylvania, (US)
LEGAL REPRESENTATIVE:
Dowden, Marina et al (76001), Elkington and Fife Prospect House, 8 Pembroke Road, Sevenoaks, Kent TN13 1XR, (GB)
PATENT (CC, No, Kind, Date): EP 524764 A1 930127 (Basic)
EP 524764 B1 960103

APPLICATION (CC, No, Date): EP 92306482 920715;
PRIORITY (CC, No, Date): US 733498 910722
DESIGNATED STATES: DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61B-017/22;
CITED PATENTS (EP A): EP 338965 A; US 4923462 A; EP 183400 A; EP 347098 A
ABSTRACT EP 524764 A1
An intravascular catheter system has a catheter with a rotating tip and a fluid path to permit fluid to be ejected around the tip for cooling the tip. The system has an electric motor for rotating the catheter tip and a second motor for controlling the fluid flow. A control circuit sets the speed of the two motors and also monitors the speed and other parameters for operational errors. If an error is detected for either motor, the entire system, including both motors, is automatically shut down. The control circuit utilizes two processors, a main processor for system control and speed control of both motors and a slave processor for monitoring the speed of the catheter motor. The main processor provides data regarding desired speed to the catheter motor and to the slave processor and the slave processor provides signals the main processor when it detects a speed error. (see image in original document)
ABSTRACT WORD COUNT: 156

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	930127	A1	Published application (A1with Search Report ;A2without Search Report)
Examination:	930512	A1	Date of filing of request for examination: 930309
Examination:	941109	A1	Date of despatch of first examination report: 940923
Change:	950510	A1	Representative (change)
Grant:	960103	B1	Granted patent
*Assignee:	960228	B1	Proprietor of the patent (transfer of rights): Theratek International, Inc. (1889801) 14740 NW 60th Avenue Miami Lakes, Florida 33014 (US) (applicant designated states: DE;FR;GB;IT)
*Assignee:	960228	B1	Previous applicant in case of transfer of rights (change): DOW CORNING WRIGHT CORPORATION (742640) P.O. Box 100 5677 Airline Road Arlington Tennessee (US) (applicant designated states: DE;FR;GB;IT)
Oppn None:	961227	B1	No opposition filed

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB96	313
CLAIMS B	(German)	EPAB96	322
CLAIMS B	(French)	EPAB96	350
SPEC B	(English)	EPAB96	12024
Total word count - document A			0
Total word count - document B			13009
Total word count - documents A + B			13009

28/5/12 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00516713
Method and catheter for controlled intravascular drug delivery .
Methode und Katheter zur kontrollierten Intravaskularwirkstoffabgabe.
Methode et catheter pour la distribution intravasculaire controlee de medicaments.
PATENT ASSIGNEE:
ADVANCED CARDIOVASCULAR SYSTEMS, INC., (456392), 3200 Lakeside Drive, Santa Clara California 95052, (US), (applicant designated states: BE;CH;DE;FR;GB;IT;LI;NL)
INVENTOR:
Gifford, Hanson S., 71 Morton Street, Palo Alto, California 94303, (US)
LEGAL REPRESENTATIVE:

Baillie, Iain Cameron et al (27951), c/o Ladas & Parry Altheimer Eck 2, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 511499 A2 921104 (Basic)
EP 511499 A3 930324
APPLICATION (CC, No, Date): EP 92105366 920327;
PRIORITY (CC, No, Date): US 679377 910402
DESIGNATED STATES: BE; CH; DE; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: A61M-025/00; A61B-005/00;
CITED PATENTS (EP A): EP 372088 A; DE 3400874 C; EP 381062 A; US 4767400 A; EP 248670 A; WO 9200113 A

ABSTRACT EP 511499 A2
A vascular perfusion catheter (10) includes a catheter body (12) having a macroporous matrix (40) forming at least a portion of its distal end. Blood flow is measured in situ by a Doppler mechanism operably coupled to the catheter body. A solution carrying a desired therapeutic agent may be introduced through the catheter and released through the macroporous matrix until a preselected blood flow is observed. (see image in original document)
ABSTRACT WORD COUNT: 73

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	921104 A2	Published application (A1with Search Report ;A2without Search Report)
Search Report:	930324 A3	Separate publication of the European or International search report
Examination:	930908 A2	Date of filing of request for examination: 930716
Change:	940831 A2	Representative (change)
Withdrawal:	950329 A2	Date on which the European patent application was deemed to be withdrawn: 941001

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	433
SPEC A	(English)	EPABF1	5385
Total word count - document A			5818
Total word count - document B			0
Total word count - documents A + B			5818

28/5/13 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00396868
Catheter and method for locally applying medication to the wall of a blood vessel or other body lumen.
Katheter und Methode zur lokal angewandten Medikation der Wand eines Blutgefasses oder eines anderen Korperlumens.
Catheter et methode pour medication appliquee localement sur la paroi d'un vaisseau sanguin ou d'une autre cavite corporelle.
PATENT ASSIGNEE:
C.R. BARD, INC., (247301), 730 Central Avenue, Murray Hill New Jersey 07974, (US), (applicant designated states: DE;ES;FR;GB;IT;NL)
INVENTOR:
Wolinsky, Harvey, 49 East 96 Street, New York, NY 10128, (US)
Barbere, Michael D., 306 Groton Street, Dunstable, Massachusetts 01827, (US)
King, Spencer L., 95 Lullwater Parkway, Atlanta, Georgia 30307, (US)
LEGAL REPRESENTATIVE:
Woodward, John Calvin et al (37981), Venner Shipley & Co. 20 Little Britain, London EC1A 7DH, (GB)
PATENT (CC, No, Kind, Date): EP 383429 A2 900822 (Basic)
EP 383429 A3 910327
EP 383429 B1 951108
APPLICATION (CC, No, Date): EP 90300438 900116;
PRIORITY (CC, No, Date): US 304352 890131

DESIGNATED STATES: DE; ES; FR; GB; IT; NL
INTERNATIONAL PATENT CLASS: A61M-025/10; A61M-031/00; A61M-029/02;
CITED PATENTS (EP A): EP 338979 A; EP 338979 A; US 4490421 A; EP 284672 A; EP 284672 A; EP 205851 A

ABSTRACT EP 383429 A2

A method and catheter for use in practising the method are provided by which a highly concentrated medication or chemotherapeutic agent can be applied locally under sufficient pressure to cause the medication or agent to penetrate into the localized tissue. The total volume of medication or agent is quite small, well below levels that might cause an adverse reaction in other parts of the body. The catheter includes a thin walled flexible **balloon** (16) having a plurality of minute holes (29) through which medication may flow at a low flow rate. The **balloon** (16) is **inflated** with the medication under pressure and the low flow rate of the order of a few ccs per minute is controlled by the minute holes (29) in the **balloon** (16). In practising the method of the invention, the **balloon** (16) is selected such that its **inflated** diameter will correspond to or be slightly greater than the diameter of the lumen into which it is to be placed so that when the **balloon** (16) is **inflated**, it will contact intimately the surface of the lumen. **Inflation** of the **balloon** (16) with the medication will cause a thin film to spread between the **balloon** (16) and the lumen, the film being maintained under a sufficient pressure to penetrate significantly the surrounding tissue with a high concentration of medication. The quantity of medication that ultimately flows free into the lumen is quite small and is insufficient to cause any other damage to the patient.

ABSTRACT WORD COUNT: 249

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	900822	A2	Published application (A1with Search Report ;A2without Search Report)
Search Report:	910327	A3	Separate publication of the European or International search report
Change:	910529	A2	Obligatory supplementary classification (change)
Examination:	911009	A2	Date of filing of request for examination: 910802
Examination:	921216	A2	Date of despatch of first examination report: 921029
Grant:	951108	B1	Granted patent
Oppn None:	961030	B1	No opposition filed

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	490
CLAIMS B	(English)	EPAB95	601
CLAIMS B	(German)	EPAB95	614
CLAIMS B	(French)	EPAB95	616
SPEC A	(English)	EPABF1	2861
SPEC B	(English)	EPAB95	2877
Total word count - document A			3351
Total word count - document B			4708
Total word count - documents A + B			8059

28/5/15 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00386626
Catheter for even distribution of therapeutic fluids.
Katheter fur eine prazise Verteilung von therapeutischen Flussigkeiten.
Catheter pour une distribution precise de fluides therapeutiques.
PATENT ASSIGNEE:
ADVANCED CARDIOVASCULAR SYSTEMS, INC., (456392), 3200 Lakeside Drive, Santa Clara California 95052, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;NL)

INVENTOR:
Sharkawy, Ahmed, 430 Southwest Parkway Nr. 2112, College Station Texas 77840, (US)
LEGAL REPRESENTATIVE:
Baillie, Iain Cameron et al (27951), c/o Ladas & Parry Altheimer Eck 2, D-80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 381062 A2 900808 (Basic)
EP 381062 A3 910605
EP 381062 B1 940323
APPLICATION (CC, No, Date): EP 90101533 900125;
PRIORITY (CC, No, Date): US 304062 890130
DESIGNATED STATES: CH; DE; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: A61M-025/00;
CITED PATENTS (EP A): DE 330284 C; US 4168703 A; DE 3314755 A; BE 689333 A; DE 1196327 C

ABSTRACT EP 381062 A2
A multilumen **vascular** catheter for the **delivery** of therapeutic fluids, e.g., containing **thrombolytic** agents, to a patient's **blood vessel** . The catheter has a plurality of flow passageways (17) in the wall of the outer tubular member (12) in which the discharge openings thereof increase in diametrical dimensions so that a desired, e.g., uniform, flow of treatment fluid is delivered exteriorly of the catheter body. The flow passageways preferably are formed by means of lasers. A first rectangularly shaped passageway is formed in the catheter wall and then a second rectangularly shaped hole is made in the wall, overlapping the first hole to form the final rectangular shape. The catheter is particularly adapced to **deliver** small quantities of **thrombolytic** agents, such as urokinase, streptokinase, and tissue plasminogen activator.
ABSTRACT WORD COUNT: 129

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	900808 A2	Published application (A1with Search Report ;A2without Search Report)
Search Report:	910605 A3	Separate publication of the European or International search report
Examination:	920108 A2	Date of filing of request for examination: 911114
Examination:	930519 A2	Date of despatch of first examination report: 930406
Grant:	940323 B1	Granted patent
Oppn None:	950315 B1	No opposition filed

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	352
CLAIMS B	(German)	EPBBF1	349
CLAIMS B	(French)	EPBBF1	384
SPEC B	(English)	EPBBF1	1762
Total word count - document A			0
Total word count - document B			2847
Total word count - documents A + B			2847

28/5/19 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00312914
Retroperfusion and retroinfusion control apparatus, system and method.
Gerat, System und Verfahren zur Steuerung der Retroperfusion und Retroinfusion.
Appareil, systeme et procede pour la commande de retroperfusion et retro-infusion.
PATENT ASSIGNEE:
RETROPERFUSION SYSTEMS, INC., (981110), 3178 Pullman Avenue, Costa Mesa California 92626, (US), (applicant designated states: DE;FR;GB;IT;SE)

INVENTOR:
Lundquist, Ingemar H., 17 Miles Drive at Dunes Road, Pebble Beach California 93953, (US)
Tarczy-Hornoch, Zoltan, 7106 Marlborough Terrace, Berkeley California 94705, (US)
Kardos, Thomas J., 1570 Via Capri, No. 10, Laguna Beach California 92651, (US)
LEGAL REPRESENTATIVE:
Cross, Rupert Edward Blount et al (42891), BOULT, WADE & TENNANT 27 Furnival Street, London EC4A 1PQ, (GB)
PATENT (CC, No, Kind, Date): EP 297723 A2 890104 (Basic)
EP 297723 A3 890503
EP 297723 B1 930825
APPLICATION (CC, No, Date): EP 88304932 880531;
PRIORITY (CC, No, Date): US 56401 870529; US 120591 871113; US 198441 880525
DESIGNATED STATES: DE; FR; GB; IT; SE
INTERNATIONAL PATENT CLASS: A61M-001/10;
CITED PATENTS (EP A): US 4493697 A; US 4648384 A; FR 2458288 A; DE 3610255 A; US 4459977 A; GB 1444117 A

ABSTRACT EP 297723 A2
Retroperfusion control apparatus (11) for supplying arterial blood of a patient to the venous side of the patient's heart including a pump (81) having an inlet (104) and an outlet (114) and a piston (88) movable through a pump stroke for moving a liquid from the inlet (104) to the outlet (114) of the pump (81). A stepper motor (47) is provided which drives the piston (81). Electronic circuitry is provided for driving the stepper motor (47) and senses the presence of an R wave in a patient to operate the stepper motor (47) in response to the sensed R wave.
ABSTRACT WORD COUNT: 105

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	890104 A2	Published application (Alwith Search Report ;A2without Search Report)
Search Report:	890503 A3	Separate publication of the European or International search report
Examination:	900321 A2	Date of filing of request for examination: 891103
Examination:	900606 A2	Date of despatch of first examination report: 900424
Grant:	930825 B1	Granted patent
Lapse:	940420 B1	Date of lapse of the European patent in a Contracting State: SE 930825
Oppn None:	940817 B1	No opposition filed
Lapse:	991020 B1	Date of lapse of European Patent in a contracting state (Country, date): IT 19930825, SE 19930825,

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1050
CLAIMS B	(German)	EPBBF1	438
CLAIMS B	(French)	EPBBF1	510
SPEC B	(English)	EPBBF1	14787
Total word count - document A			0
Total word count - document B			16785
Total word count - documents A + B			16785

28/5/20 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00308085
Catheter and guidewire exchange system.
Katheter und System zum Auswechseln eines Fuhrungsdrahtes.
Systeme d'echange de catheter et fil de guidage.

PATENT ASSIGNEE:
C.R. BARD, INC., (247300), 731 Central Avenue, Murray Hill New Jersey 07974, (US), (applicant designated states: BE;CH;DE;ES;FR;GB;IT;LI;NL)
INVENTOR:
Crittenden, James Frederick, 232 Worcester Road, Hollis New Hampshire 03049, (US)
Barbere, Michael David, 306 Groton Street, Dunstable Massachusetts 01827, (US)
White, Bryan John, 28 Thorndike Road, Lowell Massachusetts 01852, (US)
LEGAL REPRESENTATIVE:
Woodward, John Calvin et al (37981), Venner Shipley & Co. 20 Little Britain, London EC1A 7DH, (GB)
PATENT (CC, No, Kind, Date): EP 282143 A1 880914 (Basic)
EP 282143 B1 930915
APPLICATION (CC, No, Date): EP 88300026 880105;
PRIORITY (CC, No, Date): US 19644 870227
DESIGNATED STATES: BE; CH; DE; ES; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: A61M-025/00;
CITED PATENTS (EP A): US 4175564 A; US 3853130 A; US 4573970 A; GB 2127294 A

ABSTRACT EP 282143 A1
A catheter and guidewire exchange system in which the guidewire (14) is contained within a guidewire lumen in the indwelling portion of the catheter (10) and with the guidewire and catheter being separated externally of the patient. The catheter includes a guidewire lumen which is slit longitudinally (28) along the length of the catheter. The guide member (59) is carried by the catheter and serves to spread the slit of the lumen to guide the guidewire into or out of the slit guidewire lumen. The guide member may be advanced along the catheter and guidewire in zipper-like fashion so that the proximal ends of the guidewire and catheter will be separated while the distal portions will be merged.
ABSTRACT WORD COUNT: 122

LEGAL STATUS (Type, Pub Date, Kind, Text):

Application:	880914 A1	Published application (A1with Search Report ;A2without Search Report)
Examination:	881228 A1	Date of filing of request for examination: 881028
Examination:	900725 A1	Date of despatch of first examination report: 900611
Grant:	930915 B1	Granted patent
Lapse:	940629 B1	Date of lapse of the European patent in a Contracting State: BE 930915
Oppn None:	940907 B1	No opposition filed
Lapse:	950111 B1	Date of lapse of the European patent in a Contracting State: BE 930915, CH 940131, LI 940131
Lapse:	950111 B1	Date of lapse of the European patent in a Contracting State: BE 930915, CH 940131, LI 940131

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1264
CLAIMS B	(German)	EPBBF1	1192
CLAIMS B	(French)	EPBBF1	1450
SPEC B	(English)	EPBBF1	3953
Total word count - document A			0
Total word count - document B			7859
Total word count - documents A + B			7859

28/5/22 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00464714 **Image available**

PERFUSION BALLOON **AND RADIOACTIVE WIRE DELIVERY SYSTEM**
BALLONNET DE PERFUSION ET DISPOSITIF D'ADMINISTRATION A FIL RADIOACTIF
Patent Applicant/Assignee:
SCIMED LIFE SYSTEMS INC,
Inventor(s):
HASTINGS Roger N,
URICK Michael J,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9855179 A1 **19981210**
Application: WO 98US10235 19980519 (PCT/WO US9810235)
Priority Application: US 97482 19970603
Designated States: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61N-005/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 10450
English Abstract
This invention is a catheter (320) capable of irradiating **blood vessel** walls to inhibit **restenosis** after **angioplasty** . Catheters (320) are capable of simultaneous irradiation, **angioplasty** , and in some devices **drug infusion** . Preferred catheters (320) include a helical **perfusion balloon** (336) having strand windings (346) spaced apart when **inflated** , and defining a perfusion lumen (356) within. A tubular sheath (374) over the helical strands (346), and distal shaft region (326) is used in some embodiments and defines an outer wall for the perfusion lumen (356). A spiral, inter-strand space (376) is defined between the sheath outer wall, and the blood vessel inner wall providing a confined volume for controlled **delivery** of **drugs** to the vessel wall in conjunction with irradiation. A device having a radiation wire distally closed end tube is provided. A device having a radiation wire open ended tube terminating proximally of the perfusion lumen is also provided.

French Abstract
L'invention concerne ùn catheter (320) pouvant irradier les parois du vaisseau sanguin pour inhiber une restenose apres une **angioplastie** . Les catheters (320) de l'invention peuvent a la fois effectuer une irradiation, une **angioplastie** et, dans certains dispositifs, une infusion de medicaments. Des catheters preferes (320) incluent un ballonnet de perfusion (336) muni d'enroulements de fils (346) espaces lorsque le ballonnet est gonfle et delimitant une lumiere de perfusion (356) placee a l'interieur. Une gaine tubulaire (374) recouvrant les fils spirales (346) et une partie de manchon distale (326) est utilisee dans certaines formes de realisation et delimite une paroi externe pour la lumiere de perfusion (356). Un espace spirale (376) entre les fils est delimite entre la paroi externe de la gaine et la paroi interne du vaisseau sanguin et presente un volume captif pour combiner un apport regule de medicaments a la paroi vasculaire et une irradiation. L'invention concerne en outre un dispositif comprenant un tube terminal a fil radioactif et fermeture distale; elle concerne enfin un dispositif comprenant un tube extensible a fil radioactif arrivant a proximite de la lumiere de perfusion.

28/5/23 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00458401
INTRAVENOUS INFUSION SYSTEM
SYSTEME DE PERFUSION INTRAVEINEUSE
Patent Applicant/Assignee:
INNOVATIVE DESIGN ASSOCIATES,
Inventor(s):
HADZIC Admir,
VLOKA Jerry Darius,

Patent and Priority Information (Country, Number, Date):
  Patent: WO 9848865 A2 **19981105**
  Application: WO 98US5756 19980325 (PCT/WO US9805756)
  Priority Application: US 97823064 19970331
Designated States: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-005/00
Publication Language: English
Fulltext Availability:
  Detailed Description
  Claims
Fulltext Word Count: 5846
English Abstract
An intravenous fluid infusion system (10) that includes a dual-sight drip chamber (20). The infusion system (10) allows for improved, inexpensive convenient administration of IV fluids during anesthesia, and surgery using the principles with which practicing anesthesia providers are most comfortable with.

French Abstract
La presente invention concerne un systeme d'injection intraveineuse de fluide comprenant une chambre de goutte-a-goutte a deux cotes. Ce systeme de perfusion permet l'administration facile, bon marche et amelioree de fluides intraveineux au cours d'une anesthesie et d'une operation, utilisant les principes avec lesquels les anesthesistes sont le plus a l'aise dans leur pratique.

28/5/29 (Item 8 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00413738 **Image available**
SYSTEM AND METHOD OF USE FOR REVASCULARIZING STENOTIC **BYPASS GRAFTS AND OTHERS** BLOOD VESSELS
SYSTEME ET METHODE POUR REVASCULARISER DES PONTAGES ET AUTRES VAISSEAUX SANGUINS STENOSES
Patent Applicant/Assignee:
  KENSEY NASH CORPORATION,
Inventor(s):
  NASH John E,
Patent and Priority Information (Country, Number, Date):
  Patent: WO 9804199 A1 **19980205**
  Application: WO 97US13137 19970725 (PCT/WO US9713137)
  Priority Application: US 96690438 19960726
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: A61B-017/22
Publication Language: English
Fulltext Availability:
  Detailed Description
  Claims
Fulltext Word Count: 9836

English Abstract
A system and method for opening a lumen in an **occluded blood vessel**, e.g., a **coronary** bypass graft, of a living being. The system comprises an atherectomy catheter having a working head, e.g., a rotary impacting impeller, and a debris extraction sub-system. The atherectomy catheter is located within a guide catheter. The working head is arranged to operate on, e.g., impact, the occlusive material in the occluded vessel to open a lumen therein, whereupon some debris may be produced. The debris extraction sub-system introduces an infusate liquid at a first flow rate adjacent the working head and withdraws that liquid and some blood at a second and higher **flow rate**, through the guide **catheter**

to create a differential flow adjacent the working head, whereupon the debris is withdrawn in the infusate liquid and blood for collection outside the being's body. The introduction of the infusate liquid may also be used to establish an unbalanced flow adjacent the working head to enable the atherectomy catheter to be steered hydrodynamically. A guide wire having an **inflatable balloon** on its distal end may be used with the atherectomy catheter to block the flow of debris distally, while enabling distal tissues to be perfused with an oxygenating liquid.

French Abstract

Systeme et methode permettant d'ouvrir une lumiere dans un vaisseau sanguin bouche, par exemple dans un pontage coronaire, chez un etre vivant. Le systeme comprend un catheter d'atherectomie comportant une tete de travail, telle qu'un rotor d'impaction, et un sous-systeme extracteur de debris. Le catheter d'atherectomie est dispose a l'interieur d'un catheter guide. La tete de travail est configuree de facon a travailler par impaction, par exemple, le materiau obstructeur bouchant le vaisseau, de facon a y ouvrir une lumiere, ce qui est susceptible de produire des debris. Le sous-systeme extracteur de debris introduit un solute intraveineux, a un premier debit, a proximite de la tete de travail; et, par le catheter guide, il retire ledit liquide associe a un peu de sang, a un second debit, superieur au premier, de facon a produire un flux differentiel a proximite de la tete de travail, ce qui permet de retirer les debris dans le solute et le sang et de les recueillir a l'exterieur de l'organisme. L'introduction du solute peut egalement etre utilisee pour creer un flux non equilibre a proximite de la tete de travail, de facon a pouvoir commander de maniere hydrodynamique le catheter d'atherectomie. Un guide metallique comportant un ballonnet gonflable a son extremite distale peut etre utilise avec le catheter d'atherectomie pour bloquer le flux de debris au niveau distal, tout en perfusant les tissus distaux avec un liquide oxygenant.

28/5/31 (Item 10 from file: 349)

00396973 **Image available**

MULTICHANNEL CATHETER

CATHETER A PLUSIEURS CANAUX

Patent Applicant/Assignee:
ENDOSCOPIC TECHNOLOGIES INC,
BERTOLERO Arthur A,
BERTOLERO Raymond S,
RIEBMAN Jerome B,

Inventor(s):
BERTOLERO Arthur A,
BERTOLERO Raymond S,
RIEBMAN Jerome B,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9737716 A1 **19971016**
Application: WO 97US6533 19970410 (PCT/WO US9706533)
Priority Application: US 9614922 19960410; US 96766384 19961206
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: A61M-029/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 15229

English Abstract

This invention is a single, multichannel catheter useful for extracorporeal circulation of blood to a patient undergoing

cardiovascular treatments or surgery. The catheter has three independent channels and an expandable **balloon** at one end of the catheter. The first channel (34) is the largest and is of a size that allows for delivery of blood to a patient in an amount sufficient to maintain the patient's metabolism and perfusion throughout the treatment or surgery. A second channel (36), smaller than the first, is integrated into the wall of the first channel, and is suitable for delivering a biologically active fluid (e.g., for cardioplegia) to the heart and/or venting the left heart. A third channel (38), also smaller than the first, is integrated into the wall of the first channel, and suitable for delivering a fluid to the **balloon** for its expansion when positioned in the ascending aorta to occlude the flow of blood to the heart. It is important that the first channel accounts for at least about 70 % of the total channel volume. The catheter provides an improved means of performing cardiovascular surgery on a patient using a cardiopulmonary machine for extracorporeal circulation of blood. The catheter is particularly useful for cardiac surgery. The multichannel catheter is best prepared using an extrusion molding technique.

French Abstract

Cette invention concerne un catheter unique a plusieurs canaux, utilise pour la circulation extracorporelle du sang chez un patient subissant un traitement ou une operation cardio-vasculaires. Le catheter comporte trois canaux independants et un ballonnet gonflable a une extremite. Le premier canal (34) est le plus grand et sa dimension lui permet d'amener le sang dans l'organisme d'un patient en une quantite suffisante pour maintenir le metabolisme du patient et l'irrigation sanguine durant tout le traitement ou toute l'intervention. Un deuxieme canal (36), plus petit que le premier, est integre dans la paroi du premier canal et sert a amener un fluide biologique actif (p. ex. dans le cas d'une cardioplegie) vers le coeur et/ou vider le coeur gauche. Un troisieme canal (38), egalement plus petit que le premier, est integre dans la paroi du premier canal, et sert a amener un fluide dans le ballonnet pour que celui-ci puisse se gonfler lorsqu'il est place dans l'aorte ascendante afin de bloquer l'ecoulement sanguin en direction du coeur. Il est important que le premier canal represente au moins 70 % du volume total des canaux. Le catheter presente constitue un instrument ameliore qui permet d'effectuer une intervention cardio-vasculaire sur un patient au moyen d'une machine cardio-pulmonaire utilisee pour permettre la circulation extracorporelle du sang. Ce catheter est particulierement utile lors d'operations cardiaques. La meilleure facon d'obtenir un catheter a plusieurs canaux est de faire appel a une technique de moulage par extrusion.

28/5/32 (Item 11 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

00380702 **Image available**

VASCULAR IRRIGATION SOLUTION AND METHOD FOR INHIBITION OF PAIN, INFLAMMATION, SPASM AND RESTENOSIS

SOLUTION D'IRRIGATION VASCULAIRE ET METHODE D'INHIBITION DE LA DOULEUR, DE L'INFLAMMATION, DU SPASME ET DE LA RESTENOSE

Patent Applicant/Assignee:
OMEROS MEDICAL SYSTEMS INC,
DEMOPULOS Gregory A,
PIERCE Pamela Anne,
HERZ Jeffrey M,
Inventor(s):
DEMOPULOS Gregory A,
PIERCE Pamela Anne,
HERZ Jeffrey M,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9721445 A1 **19970619**
Application: WO 96US10954 19960626 (PCT/WO US9610954)
Priority Application: WO 95US16028 19951212
Designated States: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ

PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG
AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL
PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Main International Patent Class: A61K-038/08
International Patent Class: A61K-38:55
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 29611

English Abstract
A method and solution for perioperatively inhibiting a variety of pain, inflammation, spasm and **restenosis** processes resulting from cardiovascular or general **vascular** therapeutic and diagnostic procedures. The solution preferably includes multiple pain and inflammation inhibitory agents and spasm inhibitory agents at dilute concentration in a physiologic carrier, such as saline or lactated Ringer's solution. Specific preferred embodiments of the solution of the present invention for use in cardiovascular and general **vascular** procedures also include anti- **restenosis** agents. The solution is introduced luminally to continuously irrigate an **arterial** site during an operative/interventional or diagnostic procedure for preemptive inhibition of pain and inflammation, **vascular** and non- **vascular** smooth muscle spasm, and **restenosis** while avoiding undesirable side effects associated with oral, intramuscular, subcutaneous or intravenous application of larger doses of the agents. One preferred solution to inhibit pain, inflammation, vasospasm and restenosis includes a serotonin2 antagonist, a cyclooxygenase inhibitor, an endothelin antagonist, an ATP-sensitive K+ channel antagonist, a Ca2+ channel antagonist, a nitric oxide donor, an anti-thrombin agent, a glycoprotein IIb/IIIa receptor blocker, a PKC inhibitor and a protein tyrosine kinase inhibitor.

French Abstract
Methode et solution permettant d'inhiber en peri-operatoire une variete de douleurs, d'inflammations, de spasmes et de processus de restenose dus a des interventions therapeutiques et diagnostiques cardio-vasculaires ou vasculaires generales. La solution comprend de preference de multiples agents antalgiques et anti-inflammatoires, ainsi que des agents antispasmodiques, dilues dans un support physiologique, tel qu'un solute salin ou un solute lactate de Ringer. Les modes de realisation specifiques preferes de ladite solution destinee aux interventions cardio-vasculaires et vasculaires generales comprennent egalement des agents anti-restenose. On introduit la solution dans la lumiere vasculaire de facon a irriguer en continu un site arteriel durant une intervention therapeutique ou diagnostique, afin d'inhiber preventivement la douleur et l'inflammation, les spasmes des muscles lisses vasculaires et non vasculaires et la restenose, tout en evitant les effets secondaires indesirables associes a l'administration orale, intramusculaire, sous-cutanee ou intraveineuse de doses relativement importantes de ces agents. Une solution preferee pour inhiber la douleur, l'inflammation, les spasmes vasculaires et la restenose comprend un antagoniste de la serotonine, un inhibiteur de la cyclo-oxygenase, un antagoniste de l'endotheline, un antagoniste des canaux potassiques dependants de l'ATP, un antagoniste des canaux calciques, un donneur d'oxyde nitrique, un agent antithrombique, un agent bloquant les recepteurs IIb/IIIa des glycoproteines, un inhibiteur de la proteine-kinase C et un inhibiteur de la proteine tyrosine-kinase.

28/5/33 (Item 12 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00376356 **Image available**
BALLOON **CATHETER FOR DRUG APPLICATION**
CATHETER A BALLONNET POUR L'APPLICATION DE MEDICAMENTS

Patent Applicant/Assignee:
C R BARD INC,
Inventor(s):
ENGER Christine D,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9717099 A1 **19970515**
Application: WO 96US17434 19961029 (PCT/WO US9617434)
Priority Application: US 95553973 19951106
Designated States: JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-025/10
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5738

English Abstract
A method, and an apparatus for use in practicing the method, are provided by which a highly concentrated medication or chemotherapeutic agent can be applied locally under sufficient pressure to cause the medication or agent to penetrate into localized tissue or a body lumen. The total volume of medication or agent is quite small, well below levels that might cause an adverse reaction in other parts of the body. The catheter includes a thin wall flexible **balloon** having two collars and a central region between the collars, when the central regions defines a plurality of regularly spaced minute perforations through which medication may weep at a controlled, low flow rate. The flow rate is controlled by the minute perforations and the diameter of the central region is less than the diameter of the collars. In practicing the method of the invention, the **balloon** is selected such that the **inflated** diameter of the collars will correspond to or be slightly greater than the diameter of lumen into which the **balloon** is placed, and the central region will be slightly less than that lumen diameter, thereby defining a distinct, annular medication reservoir between the **balloon** and body lumen. The depth of the reservoir reduces the risk of medicine jetting against the vessel lumen if excess pressure is applied. **Inflation** of the **balloon** with a medication will cause the medication to weep from the central region of the **balloon** , consequently filling the reservoir and bathing the lumen walls. After a predetermined time, a sufficient amount of medication will be absorbed by the lumen walls and the **balloon** will be deflated so that the catheter may be withdrawn from the lumen. The quantity of medication that ultimately flows into the vessel lumen is sufficiently small so as to not cause any other systemic damage to the patient.

French Abstract
L'invention porte sur un procede et l'appareil associe au moyen desquels un medicament fortement concentre ou un agent chimiotherapeutique peuvent etre appliques localement sous une pression suffisamment elevee pour leur permettre de penetrer dans un tissu cible ou un orifice corporel. Le volume total de medicament ou d'agent est tres faible et notablement inferieur aux doses susceptibles de provoquer une reaction adverse dans d'autres parties du corps. Le catheter comporte un ballonnet souple a paroi mince comportant deux colliers et une zone centrale situee entre les colliers et percee d'une serie de perforations minuscules regulierement espaces par lesquels le medicament peut suinter avec un debit donne tres faible. La regulation du debit resulte de la taille des perforations, le diametre de la region centrale etant inferieur a celui des colliers. Le ballonnet est choisi de maniere a ce que le diametre des colliers une fois gonfles soit egal ou legerement superieur a celui de la lumiere ou l'on place le ballonnet, et que celui de la zone centrale lui soit legerement inferieur. On constitue ainsi un reservoir annulaire separe de medicament entre le ballonnet et le corps de la lumiere. L'epaisseur du reservoir reduit le risque de projection du medicament contre la lumiere du vaisseau en cas de pression trop forte. Lorsqu'on gonfle le ballonnet a l'aide d'un medicament, ce dernier suinte de la zone centrale du ballonnet, remplit le reservoir et baigne les parois de la lumiere. Apres un temps donne, les parois de la lumiere ayant absorbe une quantite suffisante de medicament, on degonfle le ballonnet pour

pouvoir extraire le catheter de la lumiere. La quantite de medicament passant finalement dans la lumiere du vaisseau est suffisamment faible pour ne causer aucun autre dommage systemique au patient.

28/5/34 (Item 13 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00357832 **Image available**
INFUSION SLEEVE CATHETER HAVING DISTAL DISTRIBUTION MANIFOLD
SONDE A MANCHON DE PERFUSION POSSEDANT UN COLLECTEUR DE DISTRIBUTION DISTAL
Patent Applicant/Assignee:
LOCALMED INC,
Inventor(s):
KLEIN Enrique J,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9640346 A1 **19961219**
Application: WO 96US7489 19960522 (PCT/WO US9607489)
Priority Application: US 95473800 19950607
Designated States: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-029/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 4516

English Abstract
An infusion catheter (10) for use in combination with a **balloon** catheter comprises a shaft and a radially expansible infusion sleeve (12) attached to a distal end of the shaft. A manifold structure (14) connects a lumen within the shaft (16) to a plurality of lumens formed over the infusion sleeve (12). A **balloon** entry port (56) is provided at a proximal end of the infusion sleeve (12) to receive the **balloon** (B) of the **balloon** catheter (BC). The infusion catheter (10) and **balloon** catheter (BC) are introduced to a target location within a body lumen, typically a target site within a coronary artery, simultaneously. After use of the **balloon** catheter (BC) to treat the body lumen in a conventional manner, the expansible sleeve of the infusion catheter (10) may be advanced over the **balloon** (B), which is then **inflated** . An infuser is delivered through a delivery lumen in the shaft (16) to a plurality of infusion lumens (26) on the radially expanded sleeve while the **balloon** (B) remains **inflated** with the **infuser** exiting **drug deliveryports** (28) near the distal ends of the **infusion** lumens (26).

French Abstract
Sonde de perfusion (10) utilisable en association avec une sonde a ballonnet, et comportant une tige et un manchon de perfusion (12) expansible dans le sens radial et fixe a une extremite distale de la tige. Une structure formant collecteur (14) relie une lumiere interieure de la tige (16) a plusieurs lumieres formees sur le manchon de perfusion (12). Un orifice (56) d'introduction du ballonnet est prevu a l'extremite proximale du manchon de perfusion (12) pour recevoir le ballonnet (B) de la sonde a ballonnet (BC). On place simultanement la sonde de perfusion (10) et la sonde a ballonnet (BC) au niveau d'un site cible a l'interieur d'une lumiere corporelle, en general a l'interieur d'une artere coronaire. Apres l'utilisation de la sonde a ballonnet (BC) pour un traitement classique de la lumiere corporelle, on peut faire avancer le manchon expansible de la sonde de perfusion (10) par-dessus le ballonnet (B), puis gonfler ce dernier. On fait passer une solution intraveineuse dans une lumiere d'administration menagee dans la tige (16) pour la faire parvenir a plusieurs lumieres de perfusion (26) sur le manchon agrandi radialement, pendant que le ballonnet (B) demeure a l'etat gonfle et que la solution sort des orifices (28) d'administration de medicament situes a proximite des extremites distales des lumieres de perfusion (26).

28/5/36 (Item 15 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00350374 **Image available**
RADIOGRAPHIC CONTRAST MATERIAL INJECTOR
INJECTEUR DE PRODUIT DE CONTRASTE RADIOGRAPHIQUE
Patent Applicant/Assignee:
INVASATEC INC,
Inventor(s):
WILSON Robert F,
LIU Jivan,
BAILIN Steven J,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9632887 A1 **19961024**
Application: WO 96US5423 19960419 (PCT/WO US9605423)
Priority Application: US 95425300 19950420; US 95426148 19950420
Designated States: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61B-006/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 8957

English Abstract
An angiographic injector system (10) includes a motor driven pump (18) which delivers radiographic contrast material to a **catheter** (30) at a variable **flow rate** which is interactively controlled by a user. Operation of the pump (18) is controlled by the user, through a user actuated remote control (14). The angiographic system (10) also includes a manifold (26) and a valve which selectively connects either a syringe pump (18) or a low pressure system (38) to a catheter (30) which is inserted into a patient. The valve is normally biased to a state which connects the low pressure system (38) to the catheter (30) for pressure monitoring, saline flushing, or aspirating functions. When an injection is to be made, the valve automatically switches so that the low pressure system (38) is disconnected and not exposed to high pressure, while the syringe pump (18) is connected through the manifold (26) to the catheter (30).

French Abstract
La presente invention concerne un systeme (10) d'injection angiographique, comprenant une pompe (18) entrainee par un moteur, qui fournit un produit de contraste radiographique a un catheter (30), avec un debit variable commande de facon interactive par un utilisateur. Le fonctionnement de la pompe (18) est commande par l'utilisateur au moyen d'un dispositif de telecommande (14). Le systeme angiographique (10) comprend aussi une tubulure (26) et une soupape qui relie de facon selective soit une pompe de seringue (18), soit un systeme a basse pression (38) a un catheter (30) qui est introduit dans un patient. La soupape est normalement dans une position ou le systeme a basse pression (38) est relie au catheter (30) aux fins de surveillance de la pression, purge par une solution saline ou aspiration. Quand une injection va etre effectuee, la soupape change de position automatiquement, de telle sorte que le systeme a basse pression (38) est debranche et ne subit pas de pression elevee, tandis que la pompe de la seringue (18) est reliee au catheter (30) par la tubulure (26).

28/5/38 (Item 17 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00347551 **Image available**
MULTIPLE HOLE DRUG DELIVERY BALLOON

BALLONNET D'ADMINISTRATION DE MEDICAMENTS A ORIFICES MULTIPLES
Patent Applicant/Assignee:
BOSTON SCIENTIFIC CORPORATION,
Inventor(s):
ROPIAK Susan M,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9630064 A1 **19961003**
Application: WO 96US4361 19960329 (PCT/WO US9604361)
Priority Application: US 95414650 19950331
Designated States: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-005/00
International Patent Class: A61M-25:00; A61M-29:00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5033

English Abstract
An **inflatable** medical device (10) for delivery of medication to an organ in the body having a multi-lumen catheter (12) and a hollow, **inflatable** channel-like medication deliverable **balloon** (14) at the distal end of the catheter. A plurality of conduits (32) extend along the **balloon** between the walls (42, 44) of the **balloon** for delivery of medications. Each conduit includes an array (40) of closely spaced apertures for allowing medications in the conduits to transfer out of the conduits into a surrounding vessel after the **balloon** is **inflated** .

French Abstract
Instrument medical (10) gonflable destine a administrer des medicaments a un organe du corps, pourvu d'un catheter (12) a plusieurs lumieres et d'un ballonnet (14) d'administration de medicaments en forme de canal, creux, gonflable et situe a l'extremite distale du catheter. Une pluralite de conduits (32) s'etendent le long du ballonnet entre les parois (42, 44) de celui-ci afin d'administrer des medicaments. Chaque conduit comporte un ensemble (40) d'ouvertures faiblement espacees les unes des autres afin de permettre aux medicaments se trouvant dans les conduits de se transferer de ces derniers a un recipient les entourant apres le gonflage du ballonnet.

28/5/39 (Item 18 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00336721
IRRIGATION SOLUTION AND METHOD FOR INHIBITION OF PAIN, INFLAMMATION AND SPASM
SOLUTION D'IRRIGATION ET PROCEDE D'INHIBITION DE LA DOULEUR, DE L'INFLAMMATION ET DES SPASMES
Patent Applicant/Assignee:
OMEROS MEDICAL SYSTEMS INC,
DEMOPULOS Gregory A,
PIERCE Pamela Anne,
HERZ Jeffrey M,
Inventor(s):
DEMOPULOS Gregory A,
PIERCE Pamela Anne,
HERZ Jeffrey M,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9619233 A2 **19960627**
Application: WO 95US16028 19951212 (PCT/WO US9516028)
Priority Application: US 94353775 19941212
Designated States: AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN KE LS MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

Main International Patent Class: A61K-038/08
International Patent Class: A61K-38:55; A61K-38:55; A61K-38:08; A61K-31:675 ; A61K-31:535; A61K-31:48; A61K-31:445; A61K-31:44; A61K-31:40; A61K-31:165; A61K-31:135; A61K-38:08; A61K-31:535; A61K-31:495; A61K; A61K; A61K; A61K; A61K
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 17581

English Abstract

A method and solution for perioperatively inhibiting a variety of pain and inflammation and spasm processes at a wound. The solution includes multiple pain and inflammation inhibitory agents and spasm inhibitory agents at dilute concentration in a physiologic base, such as saline or lactated Ringer's solution. Depending on the application, the pain and inflammation agents included in the solution may include: (1) serotonin receptor antagonists; (2) serotonin receptor agonists; (3) histamine receptor antagonists; (4) bradykinin receptor antagonists; (5) kallikrein inhibitors; (6) tachykinin receptor antagonists, including neurokinin1 and neurokinin2 receptor subtype antagonists; (7) calcitonin gene-related peptide (CGRP) receptor antagonists; (8) interleukin receptor antagonists; (9) inhibitors of enzymes active in the synthetic pathway for arachadonic acid metabolites, including (a) phospholipase inhibitors, including PLA2 isoform and PLC'gamma' isoform inhibitors, (b) cyclooxygenase inhibitors, and (c) lipooxygenase inhibitors; (10) prostanoid receptor antagonists including eicosanoid EP-1 and EP-2 receptor subtype antagonists and thromboxane receptor subtype antagonists; (11) leukotriene receptor antagonists including leukotriene B4 and D4 receptor subtype antagonists; (12) opioid receptor agonists, including mu-opiate, delta-opiate, and kappa-opiate receptor sybtype agonists; (13) purinoceptor agonists and antagonists including P2X receptor antagonists and P2Y receptor agonists; (14) adenosine triphosphate (ATP)-sensitive potassium channel openers; and (15) calcium channel antagonists. Suitable anti-inflammatory/anti-pain agents which also act as anti-spasm agents include serotonin receptor antagonists, tachykinin receptor antagonists, ATP-sensitive potassium channel openers and calcium channel antagonists. Other agents which may be utilized in the solution specifically for their anti-spasm properties including endothelin receptor antagonists and the nitric oxyde donors (enzyme activators). The solution is used to continuously irrigate a wound during an operative/interventional procedure for preemptive inhibition of pain and inflammation, as well as vascular and smooth muscle spasm, while avoiding undesirable side effects associated with oral, intramuscular or intravenous application of larger doses of the agents. The solution is useful for arthroscopic, intravascular and urologic procedures, as well as for application to burns, and intra- and postoperative application to surgical wounds.

French Abstract

Procede et solution d'inhibition perioperatoire d'une variete de types de douleurs, d'inflammations et de spasmes au niveau d'une blessure. La solution comprend de multiples agents d'inhibition de la douleur et de l'inflammation, ainsi que des agents d'inhibition des spasmes en concentration diluee dans une base physiologique, telle qu'une solution saline ou lactee de Ringer. En fonction de l'utilisation, les agents contre la douleur et l'inflammation contenus dans la solution peuvent comprendre: (1) des antagonistes du recepteur de serotonine; (2) des agonistes du recepteur de serotonine; (3) des antagonistes du recepteur d'histamine; (4) des antagonistes du recepteur de bradykinine; (5) des inhibiteurs de kallikreine; (6) des antagonistes du recepteur de tachykinine, y compris des antagonistes du sous-type du recepteur de neurokinine1 et de neurokinine2; (7) des antagonistes du recepteur du peptide apparente au gene de calcitonine (CGRP); (8) des antagonistes du recepteur d'interleukine; (9) des inhibiteurs d'enzymes actives dans la voie de synthese de metabolites d'acide arachadonique, y compris (a) des inhibiteurs de phospholipase, incluant les inhibiteurs de l'isoforme PLA2

et de l'isoforme PLC'gamma', (b) des inhibiteurs de cyclooxygenase et (c) des inhibiteurs de lipooxygenase; (10) des antagonistes du recepteur de prostanoide, y compris des antagonistes du sous-type du recepteur de EP-1 et de EP-2 eicosanoide et des antagonistes du sous-type du recepteur de thromboxane; (11) des antagonistes du recepteur des leucotrienes, y compris des antagonistes du sous-type de recepteur D4 et B4 des leucotrienes; (12) des agonistes du recepteur d'opioides, y compris des agonistes du sous-type du recepteur de mu-opiaces, de delta-opiaces et de kappa-opiaces; (13) des agonistes et antagonistes du purinocepteur, y compris des antagonistes du recepteur de P2X et des agonistes du recepteur P2Y; (14) des ouvreurs de canaux de potassium sensibles au triphosphate d'adenosine (ATP) et (15) des antagonistes de canaux de calcium. Des agents appropries anti-inflammatoires et antalgiques agissant egalement en tant qu'agents antispasmodiques comprennent des antagonistes du recepteur de serotonine, des antagonistes du recepteur de tachykinine, des ouvreurs de canaux de potassium sensibles a l'ATP et des antagonistes de canaux de calcium. D'autres agents qu'on peut utiliser dans la solution specifiquement pour leurs proprietes antispasmodiques comprennent des antagonistes du recepteur d'endotheline et des donneurs d'oxyde nitrique (activateurs d'enzymes). On utilise cette solution afin d'irriguer en continu une blessure pendant une procedure operatoire ou d'intervention afin d'inhiber prioritairement la douleur et l'inflammation, ainsi que les spasmes des muscles lisses et des muscles vasculaires, tout en evitant les effets secondaires indesirables associes a l'administration orale, intramusculaire ou intraveineuse de doses plus importantes de ces agents. Cette solution est utile dans des interventions arthroscopiques, intravasculaires et urologiques, ainsi qu'en application a des brulures et a des lesions chirurgicales intra- et post-operatoires. +/-+/-

28/5/41 (Item 20 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00308621
PERFUSION SHUNT DEVICE FOR RECEIVING ANGIOPLASTY BALLOON
DISPOSITIF DE DERIVATION DE PERFUSION POUR RECEVOIR UN BALLONNET D' ANGIOPLASTIE
Patent Applicant/Assignee:
LOCALMED INC,
Inventor(s):
KLEIN Enrique J,
BAJOR Jordan,
ALBA Paul,
KAPLAN Aaron V,
GOELD Paul K,
EVARD Philip C,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9526773 A1 **19951012**
Application: WO 95US4191 19950403 (PCT/WO US9504191)
Priority Application: US 94221613 19940401; US 94305250 19940913; US 95401541 19950310
Designated States: AU CA JP KR NZ AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-025/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 11444

English Abstract
A perfusion shunt device (10) is used in conjunction with **balloon** catheters to provide blood perfusion across an **inflated balloon** in a blood vessel. The perfusion shunt device (10) comprises a flexible conduit structure (12) having one or more blood perfusion paths (24) formed from a proximal end to a distal end thereof. The flexible conduit

structure (12) is usually attached directly or indirectly to a proximal shaft structure. Discrete anchors or expansible sleeves or cages are provided for locating the conduit structure (12) over the **balloon** on the catheter. The device may be loaded over a conventional **angioplasty balloon** catheter outside of the blood vessel being treated, either before or after an **angioplasty** procedure. In an alternative embodiment, a non-distensible pouch (312) is formed integrally with the flexible conduit structure (12) in order to receive the **balloon** of a **balloon angioplasty** catheter. The non-distensible nature of the pouch limits the **inflated balloon** size.

French Abstract

Dispositif de derivation de perfusion (10) utilise en association avec des sondes a ballonnet pour permettre une perfusion sanguine autour d'un ballonnet gonfle dans un vaisseau sanguin. Ledit dispositif de derivation de perfusion (10) comprend un conduit flexible (12) muni d'un ou de plusieurs canaux de perfusion sanguine (24) allant d'une extremite proximale a une extremite distale du conduit. Ce conduit flexible (12) est generalement fixe directement ou indirectement a un axe proximal. Des elements d'ancrage discrets ou des manchons ou cages expansibles sont prevus pour placer le conduit (12) sur le ballonnet de la sonde. Ce dispositif peut etre place sur une sonde a ballonnet pour **angioplastie** classique a l'exterieur du vaisseau sanguin en cours de traitement, soit avant soit apres une **angioplastie** . Dans un autre mode de realisation, une poche non dilatable (312) fait partie integrante du conduit flexible (12) afin de recevoir le ballonnet d'une sonde pour **angioplastie** a ballonnet. La nature non dilatable de la poche permet de limiter la taille du ballonnet gonfle.

28/5/44 (Item 23 from file: 349)

00283054

LOW PROFILE PERFUSION CATHETER

CATHETER DE PERFUSION PLAT

Patent Applicant/Assignee:
CARDIOVASCULAR DYNAMICS INC,
Inventor(s):
CROCKER Michael,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9501200 A1 **19950112**
Application: WO 94US7265 19940628 (PCT/WO US9407265)
Priority Application: US 9384820 19930630
Designated States: JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61M-029/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 10987

English Abstract

Disclosed is a low profile perfusion catheter, for use in coronary **angioplasty** applications. Preferably the catheter is provided with an **inflatable** dilatation **balloon** (28), and a perfusion lumen (12) extending therethrough. The diameter of the perfusion lumen is enlargeable from a first (37) reduced diameter to a second enlarged diameter. In one embodiment an axially movable tubular support (50) is movable within the lumen from a proximal insertion position to a distal perfusion position. In another embodiment the support (72) is radially expandable. In a further embodiment a porous **drug delivery balloon** (122) is provided.

French Abstract

Catheter de perfusion plat, destine a des applications relatives a l' **angioplastie** coronaire. Le catheter est de preference pourvu d'un

ballonnet de dilatation gonflable (28) et d'une lumiere de perfusion (12) qui le traverse. Le diametre de la lumiere peut etre elargi pour passer d'un premier diametre reduit (37) a un second diametre elargi. Selon un mode de realisation, un support tubulaire axialement mobile (50) peut etre deplace, dans la lumiere, entre une position d'insertion proximale et une position de perfusion distale. Selon un autre mode de realisation, le support (72) est radialement extensible. Selon un autre mode de realisation, un ballonnet poreux (122), destine a l'apport d'un medicament, est decrit.

28/5/52 (Item 31 from file: 349)

00202923 **Image available**

METHOD AND CATHETER FOR INTRAVASCULAR DRUG DELIVERY
PROCEDE ET CATHETER POUR ADMINISTRATION INTRAVASCULAIRE DE MEDICAMENTS

Patent Applicant/Assignee:
CARDIOVASCULAR THERAPEUTIC TECHNOLOGIES INC,
Inventor(s):
GRAOR Robert A,

Patent and Priority Information (Country, Number, Date):
Patent: WO 9200113 A1 **19920109**
Application: WO 91US4336 19910618 (PCT/WO US9104336)
Priority Application: US 90311 19900626 .
Designated States: AT BE CA CH DE DK ES FR GB GR IT JP LU NL SE
Main International Patent Class: A61M-005/00
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 5074

English Abstract
A vascular perfusion catheter (10) includes a catheter body (12) having a macroporous matrix (40) forming at least a portion of its distal end (16). A solution carrying a desired therapeutic agent may be introduced through the catheter (10) and released through the macroporous matrix (40) under controlled conditions. By forming a matrix as a tubular element (20), the therapeutic agent may be released uniformly in all radial directions over a preselected length within a blood vessel.

French Abstract
Catheter de perfusion vasculaire (10) comprenant un corps (12) dote d'une matrice macroporeuse (40) formant au moins une partie de son extremite distale (16). Une solution contenant un agent therapeutique desire peut etre introduite dans le catheter (10) et liberee a travers la matrice macroporeuse (40) dans des conditions controlees. Grace a la matrice en forme d'element tubulaire (20), l'agent therapeutique peut etre libere uniformement dans toutes les directions radiales sur une longueur preselectionnee au sein d'un vaisseau sanguin.

?

```
Set     Items   Description
S1    5872460   (VENOUS OR VEIN? OR ARTERY OR ARTERI? OR VASCULAR? OR INTR-
            ?VASC? OR INTR?VEN? OR BLOOD?()VESSEL? OR VENAL OR CORONAR?)
S2    1255251   OCCLUD? OR OCCLUSI? OR OBSTRUCT? OR STENOS? OR STENOT? OR -
            RESTENOS? OR RESTENOT? OR PLAQUE?
S3    1808262   SCLERO? OR THROMB? OR BLOODCLOT? OR BLOOD()CLOT? OR ISCHEM-
            I? OR ARTER?SCLER? OR PLAQUING
S4       4035   CALCIUM()DEPOSIT?
S5     320828   BALLOON? OR PLASTY? OR PLASTIE? ? OR ANGIOPLAST? OR OCCLU?-
            ()DEVICE? OR INFLAT? OR CARDIOPLAST?
S6        272   ARTERIOPLAST?
S7    6164227   DELIVER? OR ADMINIST? OR INJECT? OR INFUS? OR PERFUS?
S8     570193   CATHETER? OR CANNULA? OR CANULA? OR TROCAR? OR LUMEN? OR H-
            OLLOW?(N)WIRE?
S9    8729531   DRUG? OR NARCOTIC? OR OCCLU?(N)TREAT? OR ANTICOAGUL? OR AN-
            TI()COAGUL? OR THROMBYT?
S10    711989   RADIONUCLID? OR RADIO()NUCLID? OR RADIOISOTOP? OR RADIO()I-
            SOTOP? OR RADIOACTIVE()ISOTOP?
S11        50   RADIO()ACTIVE()ISOTOP?
S12    268276   FLOWRATE? OR FLOW()RATE? OR "CC" OR "C.C." OR CUBIC()CENTI-
            L?
S13   1821202   S7(10N)(S9 OR S10 OR S11)
S14       341   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6) AND S8 AND S12
S15        30   S13 AND S14
S16   2029950   S3 OR ARTERI?SCLER? OR ARTER?()SCLER? OR ARTHER?SCLER? OR -
            ARTHER?()SCLER? OR ATHER?SCLER? OR ATHER?()SCLER?
S17    320893   S5 OR (CARDIO? OR ANGIO?)()PLAST?
S18   8769279   S9 OR THROMBOL?
S19    288139   S12 OR (INFUS? OR PERFUS?)()RATE?
S20   1826721   S7(10N)(S9 OR S10 OR S11 OR S18)
S21       372   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6 OR S17) AND S8 AND (-
            S12 OR S19)
S22        50   S20 AND S21
S23    738125   S1(10N)(S2 OR S3 OR S4)
S24    321107   S5 OR S6 OR S17
S25   1826721   S7(10N)(S9 OR S10 OR S11 OR S18)
S26      2976   S8(10N)(S12 OR S19)
S27         4   S23 AND S24 AND S25 AND S26
S28         3   S27 AND PY<1999
S29    191901   DC=D1.496.749?
S30   1826725   S7(10N)(S9 OR S10 OR S11 OR S18 OR S29)
S31         4   S23 AND S24 AND S30 AND S26
S32      8333   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6 OR S17) AND S8 AND (-
            S9 OR S10 OR S11 OR S18)
S33    288139   (S12 OR S19)
S34        95   S32 AND S33
S35        95   S34 OR S31 OR S27 OR S28
S36        73   S35 AND PY<1999
S37        51   RD (unique items)
?show files
File   2:INSPEC 1969-2003/Sep W3
         (c) 2003 Institution of Electrical Engineers
File   5:Biosis Previews(R) 1969-2003/Sep W2
         (c) 2003 BIOSIS
File   6:NTIS 1964-2003/Sep W4
         (c) 2003 NTIS, Intl Cpyrght All Rights Res
File   8:Ei Compendex(R) 1970-2003/Sep W3
         (c) 2003 Elsevier Eng.  Info. Inc.
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Sep W3
         (c) 2003 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 155:MEDLINE(R) 1966-2003/Sep W4
         (c) format only 2003 The Dialog Corp.
File  73:EMBASE 1974-2003/Sep W3
         (c) 2003 Elsevier Science B.V.
File 441:ESPICOM Pharm&Med DEVICE NEWS 2003/Sep W4
         (c) 2003 ESPICOM Bus.Intell.
```

36/5,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11768689 BIOSIS NO.: 199900014798
Development of a new multifunctional balloon **device for PTCA: The performance of prototype device and** drug **delivery.**
AUTHOR: Itoh T; Noguchi T; Nonogi H; Matsuda T; Sugawara T; Arai T; Kanda K ; Tsutsui N
AUTHOR ADDRESS: Div. Cardiol., Res. Inst., Dep. Bioeng., Natl. Cardiovasc. Cent., Osaka 565**Japan
JOURNAL: Japanese Journal of Artificial Organs 27 (3):p641-646 **1998**
ISSN: 0300-0818
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Japanese; Non-English
SUMMARY LANGUAGE: Japanese; English

ABSTRACT: We have developed a new **balloon catheter** device with multifunctions: **inflation** of **coronary stenosis** , **drug** delivery, and perfusion of distal vessel and evaluated in vitro and hi vivo using canine model. This **balloon catheter** has eight perfusion ports at the proximal site of **balloon** , and a **drug** delivery port at the distal site of **balloon** . Extended **balloon** distal tube was used as **drug** delivery region. The **flow - rate** was obtained around 42 **cc** to 52 **cc** /min. The simulated **drug** was stained hi the **drug** delivery region under the low pressure in **balloon** inside with continuous infusion (1 **cc** /min.), whereas the simulated **drug** was wash out without continuous infusion. The distal perfusion % **flow - rate** was obtained 12.2+-5.9% comparing with control in a dog carotid **artery** . A continuous infusion of both FITC-labeled **drug** resulted in its local accumulation on and in a injured vessel wall, respectively. This new device may promise to realize local delivery of therapeutic agents at the **balloon** injury site after mechanical **balloon** dilatation to protect **restenosis** .

DESCRIPTORS:
MAJOR CONCEPTS: Cardiovascular System (Transport and Circulation)
BIOSYSTEMATIC NAMES: Canidae--Carnivora, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: dog (Canidae)
ORGANISMS: PARTS ETC: carotid **artery** --circulatory system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Carnivores; Chordates ; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Vertebrates
METHODS & EQUIPMENT: percutaneous transluminal **coronary angioplasty** { PTCA}--analytical method
MISCELLANEOUS TERMS: **coronary stenosis** ; **drug** delivery; prototype device
CONCEPT CODES:
14501 Cardiovascular System-General; Methods
22002 Pharmacology-General
BIOSYSTEMATIC CODES:
85765 Canidae

Development of a new multifunctional balloon **device for PTCA: The performance of prototype device and** drug **delivery.**
1998

ABSTRACT: We have developed a new **balloon catheter** device with multifunctions: **inflation** of **coronary stenosis** , **drug** delivery, and perfusion of distal vessel and evaluated in vitro and hi vivo using canine model. This **balloon catheter** has eight perfusion ports at the proximal site of **balloon** , and a **drug** delivery port at the distal site of **balloon** . Extended **balloon** distal tube was used as **drug** delivery region. The **flow - rate** was obtained around 42 **cc** to 52 **cc** /min. The simulated **drug** was stained hi the **drug** delivery region under the low pressure in **balloon** inside with continuous infusion (1 **cc** /min.), whereas the simulated **drug** was wash out without continuous infusion. The distal perfusion % **flow - rate** was obtained 12.2+-5.9% comparing

with control in a dog carotid **artery** . A continuous infusion of both FITC-labeled **drug** resulted in its local accumulation on and in a injured vessel wall, respectively. This new device may promise to realize local delivery of therapeutic agents at the **balloon** injury site after mechanical **balloon** dilatation to protect **restenosis** .
DESCRIPTORS:
ORGANISMS: PARTS ETC: carotid **artery** --
METHODS & EQUIPMENT: percutaneous transluminal **coronary** **angioplasty** (PTCA...
MISCELLANEOUS TERMS: **coronary** **stenosis** ; ...

... **drug** delivery

36/5,K/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07263378 BIOSIS NO.: 000090043254
INTRAARTERIAL UROKINASE INFUSION THERAPY FOR ARTERIAL OCCLUSIVE **DISEASE IN THE PELVIS AND EXTREMITY WITH SPECIAL REFERENCE TO SHORT TERM HIGH DOSE INFUSION**
AUTHOR: KICHIKAWA K; NISHIMINE K; UCHIDA H; KUBOTA Y; YOSHIOKA T; HONDA N; HIRAI T; TAMADA T; NISHIMURA Y; ET AL
AUTHOR ADDRESS: DEP. RADIOLOGY, NARA MEDICAL UNIVERSITY, JPN.
JOURNAL: NIPPON ACTA RADIOL 50 (3). 1990. 229-239. **1990**
FULL JOURNAL NAME: Nippon Acta Radiologica
CODEN: NHGZA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Thirty-five complete **arterial** **occlusions** of pelvis and extremity in 29 patients were treated with intraarterial urokinase infusion therapy. In 28 limbs, the **occlusions** were due to **arteriosclerotic** change and in 7 lesions, the **occlusions** were due to Burger's disease. The patients with **arteriosclerotic** change ranged in age from 52 to 84 years with a mean age of 68 years, and the patients with Burger's disease ranged in age from 35 to 47 years with a mean age of 43 years. There were 24 men and 5 women. The estimated duration of the **occlusion** was from 5 days to 5 years with a mean duration of 11 months. The length of the **occluded** segments ranged from 1 to 45 cm with a mean length of 13.9 cm. The **occlusion** was located in the iliac **artery** in 13 patients, the femoral **artery** in 11 patients, both the iliac and the femoral **artery** in 2 patients, the popliteal **artery** in 5 patients, the femoro-popliteal **artery** in 1 patient, the brachial **artery** in 2 patients and the radial **artery** in 1 patient. The infusion **catheter** was gently advanced into the proximal portion of the clot over a flexible guide wire, and urokinase was infused at a rate of 5000 .apprx. 10000 IU/min, as a short term high dose infusion (SHI), until antegrade blood flow was reestablished. The **catheter** was then withdrawn to a point proximal to all of the remaining clot, and the **infusion** **rate** was reduced to 10000 .apprx. 20000 IU/h as a continuous low dose infusion (CLI). After **thrombolytic** recanalization, a percutaneous transluminal **angioplasty** (PTA) was performed in those case which demonstrated a residual narrowing of the **lumen** . The initial success rate was 86%. Reocclusions were observed in 5 lesions (17%) and a second recanalization was successful in 2 of 3 patients. The 1-year cumulative patency rate following recanalization was 88.4% and the 2-year patency rate was 78.6%. No significant complications directly related to the procedure were observed. SHI combined with CLI and PTA appears to be an effective and safe therapy for chronic long segmental **arterial** **occlusion** .

DESCRIPTORS: HUMAN **THROMBOLYTIC - DRUG** ANTIATHEROGENIC- **DRUG** BUERGER'S DISEASE **ARTERIOSCLEROSIS**
CONCEPT CODES:
11316 Chordate Body Regions-Pelvis (1970-)
11318 Chordate Body Regions-Extremities (1970-)
12512 Pathology, General and Miscellaneous-Therapy (1971-)

14508 Cardiovascular System-Blood Vessel Pathology
22005 Pharmacology-Clinical Pharmacology (1972-)
22008 Pharmacology-Blood and Hematopoietic Agents
22010 Pharmacology-Cardiovascular System
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
14501 Cardiovascular System-General; Methods
22100 Routes of Immunization, Infection and Therapy
BIOSYSTEMATIC CODES:
86215 Hominidae
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):
Animals
Chordates
Vertebrates
Mammals
Primates
Humans

INTRAARTERIAL UROKINASE INFUSION THERAPY FOR ARTERIAL OCCLUSIVE **DISEASE IN THE PELVIS AND EXTREMITY WITH SPECIAL REFERENCE TO SHORT TERM HIGH DOSE INFUSION**
1990

ABSTRACT: Thirty-five complete **arterial occlusions** of pelvis and extremity in 29 patients were treated with intraarterial urokinase infusion therapy. In 28 limbs, the **occlusions** were due to **arteriosclerotic** change and in 7 lesions, the **occlusions** were due to Burger's disease. The patients with **arteriosclerotic** change ranged in age from 52 to 84 years with a mean age of 68...

...of 43 years. There were 24 men and 5 women. The estimated duration of the **occlusion** was from 5 days to 5 years with a mean duration of 11 months. The length of the **occluded** segments ranged from 1 to 45 cm with a mean length of 13.9 cm. The **occlusion** was located in the iliac **artery** in 13 patients, the femoral **artery** in 11 patients, both the iliac and the femoral **artery** in 2 patients, the popliteal **artery** in 5 patients, the femoro-popliteal **artery** in 1 patient, the brachial **artery** in 2 patients and the radial **artery** in 1 patient. The infusion **catheter** was gently advanced into the proximal portion of the clot over a flexible guide wire...

...as a short term high dose infusion (SHI), until antegrade blood flow was reestablished. The **catheter** was then withdrawn to a point proximal to all of the remaining clot, and the **infusion rate** was reduced to 10000 .apprx. 20000 IU/h as a continuous low dose infusion (CLI). After **thrombolytic** recanalization, a percutaneous transluminal **angioplasty** (PTA) was performed in those case which demonstrated a residual narrowing of the **lumen** . The initial success rate was 86%. Reocclusions were observed in 5 lesions (17%) and a...

...CLI and PTA appears to be an effective and safe therapy for chronic long segmental **arterial occlusion** .
DESCRIPTORS: HUMAN **THROMBOLYTIC - DRUG** ANTIATHEROGENIC- **DRUG** BUERGER'S DISEASE **ARTERIOSCLEROSIS**

36/5,K/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05553779 BIOSIS NO.: 000083026919
SHORT-TERM INTRAARTERIAL INFUSION WITH ULTRAHIGH-DOSE UROKINASE IN TREATMENT OF PERIPHERAL ARTERIAL OCCLUSIVE **DISEASE**
AUTHOR: SATO M; TERADA M; MITSUZANE K; SUWA K; YOSHIKAWA A; KISHI K; SHIRAI S; MAEDA M; SHIOYAMA Y; ET AL
AUTHOR ADDRESS: DEP. RADIOL., WAKAYAMA MED. COLL., JPN.
JOURNAL: NIPPON ACTA RADIOL 46 (8). 1986. 1001-1006. **1986**
FULL JOURNAL NAME: Nippon Acta Radiologica
CODEN: NHGZA

RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Seven patients with peripheral **arterial occlusion** (lengths: 3, 8, 10, 11, 14,17 and 20 cm) underwent short-term intraarterial infusion with ultrahigh-dose urokinase. Urokinase was administered through a 5 French **catheter** embedded into **occlusive** segment of the **artery** at a rate of 10,000 IU/min. The total volume of Urokinase used, per patient, was between 120,000 and 1,210,000 IU. Recanalization of the **occluded** segment was successful in each case. Percutaneous transluminal **angioplasty** with a Gruntzig **balloon catheter** was additionally carried out for four patients to dilate the residual **stenosis** . The treatment lasted minimally 12 and maximally 121 minutes. Treatment time was significantly reduced by short-time intraarterial infusion with high-dose urokinase through the **catheter** , deeply embedded in the clot, which **infusion rate** was more than twice as that of McNamara and Fischer. Our method brought us not only rapid recanalization and higher incidence of total clot lysis, but also minimized adverse reactions and complications, which frequently occurred during long-term indwelling of **catheters** in standard fibrinolytic regimen.

DESCRIPTORS: HUMAN **THROMBOLYTIC - DRUG STENOSIS** PERCUTANEOUS TRANSLUMINAL **ANGIOPLASTY** RECANALIZATION
CONCEPT CODES:
12512 Pathology, General and Miscellaneous-Therapy (1971-)
14508 Cardiovascular System-Blood Vessel Pathology
22005 Pharmacology-Clinical Pharmacology (1972-)
22008 Pharmacology-Blood and Hematopoietic Agents
22010 Pharmacology-Cardiovascular System
11105 Anatomy and Histology, General and Comparative-Surgery
18501 Integumentary System-General; Methods
22100 Routes of Immunization, Infection and Therapy
BIOSYSTEMATIC CODES:
86215 Hominidae
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):
Animals
Chordates
Vertebrates
Mammals
Primates
Humans

SHORT-TERM INTRAARTERIAL INFUSION WITH ULTRAHIGH-DOSE UROKINASE IN TREATMENT OF PERIPHERAL ARTERIAL OCCLUSIVE **DISEASE**
1986

ABSTRACT: Seven patients with peripheral **arterial occlusion** (lengths: 3, 8, 10, 11, 14,17 and 20 cm) underwent short-term intraarterial infusion with ultrahigh-dose urokinase. Urokinase was administered through a 5 French **catheter** embedded into **occlusive** segment of the **artery** at a rate of 10,000 IU/min. The total volume of Urokinase used, per patient, was between 120,000 and 1,210,000 IU. Recanalization of the **occluded** segment was successful in each case. Percutaneous transluminal **angioplasty** with a Gruntzig **balloon catheter** was additionally carried out for four patients to dilate the residual **stenosis** . The treatment lasted minimally 12 and maximally 121 minutes. Treatment time was significantly reduced by short-time intraarterial infusion with high-dose urokinase through the **catheter** , deeply embedded in the clot, which **infusion rate** was more than twice as that of McNamara and Fischer. Our method brought us not...

...but also minimized adverse reactions and complications, which frequently occurred during long-term indwelling of **catheters** in standard fibrinolytic regimen.
DESCRIPTORS: HUMAN **THROMBOLYTIC - DRUG STENOSIS** PERCUTANEOUS TRANSLUMINAL **ANGIOPLASTY** RECANALIZATION

36/5,K/14 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06650758 Genuine Article#: ZH211 Number of References: 23
Title: A novel method for efficient drug delivery
Author(s): Markou CP; Lutostansky EM; Ku DN; Hanson SR (REPRINT)
Corporate Source: EMORY UNIV,SCH MED, DEPT MED, DIV HEMATOL ONCOL, 1639 PIERCE DR, ROOM 1129/ATLANTA//GA/30322 (REPRINT); EMORY UNIV,SCH MED, DEPT MED, DIV HEMATOL ONCOL/ATLANTA//GA/30322; GEORGIA INST TECHNOL,GEORGE W WOODRUFF SCH MECH ENGN/ATLANTA//GA/30332
Journal: ANNALS OF BIOMEDICAL ENGINEERING, **1998** , V26, N3 (MAY-JUN), P 502-511
ISSN: 0090-6964 Publication date: 19980500
Publisher: BLACKWELL SCIENCE INC, 350 MAIN ST, MALDEN, MA 02148
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: ENGINEERING, BIOMEDICAL
Abstract: Local delivery of anti- **thrombotic** and anti- **restenotic** **drugs** is desired to achieve high concentrations of agents which may be rapidly degraded systemically or which exhibit very short half-lives in vivo. In this article, the operating characteristics of a novel local **drug** delivery method are described and its effectiveness demonstrated computationally and experimentally. Computational models used a finite volume method to determine the concentration field. Optical dye density measurements of Evans blue in saline were performed in an in vitro steady flow system. Modeling parameters were kept in the physiologic range. Experimental how visualization studies demonstrated high concentrations of infusate near the vessel wall. Computational studies predicted high, clinically significant **drug** concentrations along the wall downstream of the infusion device. When the radial infusion velocity is large (infusion **flow** **rate** , Q(inf)>0.5% of the main **flow** **rate** , Q), the wall concentration of the infused **drug** remains high, e.g., levels are greater than 80% of the infusate concentration 5 cm downstream of the infusion device. At lower **infusion** **rates** (Q(inf)<0.001Q), the **drug** concentration at the wall decreases exponentially with axial distance to less than 25% of the infusate concentration 5 cm downstream of the infusion device, although therapeutic **drug** levels are still readily maintained. The near wall **drug** concentration is a function of flow conditions, **infusion** **rate** , and the **drug** diffusivity. Good agreement was obtained between computational and experimental concentration measurements. Flow simulation and experimental results indicate that the technique can effectively sustain high local **drug** concentrations for inhibition of **thrombosis** and **vascular** lesion formation. (C) 1998 Biomedical Engineering Society.
Descriptors--Author Keywords: local **drug** delivery ; mass transfer ; blood-materials interactions
Identifiers--KeyWord Plus(R): INTIMAL HYPERPLASIA; **THROMBOSIS**; HEPARIN; INFUSION; **ANGIOPLASTY**; **CATHETER**; GRAFTS
Cited References:
BIRD RB, 1960, P42, TRANSPORT PHENOMENA
CHEN C, 1997, V67, P26, J SURG RES
CHEN C, 1997, V69, P300, J SURG RES
CHEN CY, 1996, V10, P147, ANN VASC SURG
CHEN CY, 1996, V94, P1989, CIRCULATION
CHEN CY, 1995, V22, P237, J VASC SURG
CUMBERLAND DC, 1994, V23, PA186, J AM COLL CARDIOL
CUSSLER EL, 1984, DIFFUSION
HANSON SR, 1995, V34, P383, ADV PHARMACOL
HONG MK, 1993, V4, P1023, CORONARY ARTERY DIS
LAMBERT CR, 1993, V4, P469, CORONARY ARTERY DIS
LINCOFF AM, 1994, V90, P2070, CIRCULATION
LOVICH MA, 1995, V77, P1143, CIRC RES
MA PP, 1994, V37, P2723, INT J HEAT MASS TRAN
MARKOU CP, 1996, V94, P1563, CIRCULATION
MATTAR SG, 1996, V60, P339, J SURG RES

MULLER DWM, 1990, V1, P438, CORONARY ARTERY DIS
NATHAN A, 1995, P29, MOL INTERVENTIONS LO
PINCHAK AC, 1975, V41, P646, J APPL PHYSIOL
ROGERS C, 1995, P131, MOL INTERVENTIONS LO
SAAVEDRA JE, 1996, V39, P4361, J MED CHEM
SCOTT NA, 1994, V90, P1951, CIRCULATION
WOLINSKY H, 1990, V15, P475, J AM COLL CARDIOL

Title: A novel method for efficient drug **delivery , 1998**

Abstract: Local delivery of anti- **thrombotic** and anti- **restenotic** **drugs** is desired to achieve high concentrations of agents which may be rapidly degraded systemically or...

...short half-lives in vivo. In this article, the operating characteristics of a novel local **drug** delivery method are described and its effectiveness demonstrated computationally and experimentally. Computational models used a...

...demonstrated high concentrations of infusate near the vessel wall. Computational studies predicted high, clinically significant **drug** concentrations along the wall downstream of the infusion device. When the radial infusion velocity is large (infusion **flow** **rate** , Q(inf)>0.5% of the main **flow** **rate** , Q), the wall concentration of the infused **drug** remains high, e.g., levels are greater than 80% of the infusate concentration 5 cm downstream of the infusion device. At lower **infusion** **rates** (Q(inf)<0.001Q), the **drug** concentration at the wall decreases exponentially with axial distance to less than 25% of the infusate concentration 5 cm downstream of the infusion device, although therapeutic **drug** levels are still readily maintained. The near wall **drug** concentration is a function of flow conditions, **infusion** **rate** , and the **drug** diffusivity. Good agreement was obtained between computational and experimental concentration measurements. Flow simulation and experimental results indicate that the technique can effectively sustain high local **drug** concentrations for inhibition of **thrombosis** and **vascular** lesion formation. (C) 1998 Biomedical Engineering Society.

...Identifiers--INTIMAL HYPERPLASIA; **THROMBOSIS**; HEPARIN; INFUSION; **ANGIOPLASTY**; **CATHETER**; GRAFTS

36/5,K/18 (Item 5 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03016329 Genuine Article#: MY667 Number of References: 15

Title: LOCAL INTRAMURAL DRUG **-DELIVERY USING AN INFUSION** BALLOON **FOLLOWING** ANGIOPLASTY **IN NORMAL AND ATHEROSCLEROTIC VESSELS**

Author(s): RASHEED Q; CACCHIONE JG; BERRY J; RICHARDS F; BRYANT L; STRONY J ; ENGER C; HODGSON JM
Corporate Source: UNIV HOSP CLEVELAND,DIV CARDIOL,2074 ABINGTON/CLEVELAND//OH/44106; CASE WESTERN RESERVE UNIV/CLEVELAND//OH/44106

Journal: CATHETERIZATION AND CARDIOVASCULAR DIAGNOSIS, **1994** , V31, N3 (MAR), P240-245
ISSN: 0098-6569
Language: ENGLISH · Document Type: ARTICLE
Geographic Location: USA
Subfile: SciSearch; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: CARDIOVASCULAR SYSTEM

Abstract: Local intramural delivery of various pharmacologic agents following **angioplasty** has been proposed as a means of reducing **restenosis** . This study tested whether local intramural delivery of aqueous solutions using an infusion **balloon** could be accomplished safely in normal vessels and whether such infusion was safe following standard **angioplasty** in diseased vessels. Infusion of aqueous agents into normal canine **arteries** had no adverse effect. Infusion of several aqueous agents (less-than-or-equal-to 4 **cc** at 4 atm) into

diseased swine iliac **arteries** following **balloon angioplasty** did not worsen existing or create new dissections. Histologically, infusion treated vessels did not differ in either model from vessels treated with **angioplasty** alone. We conclude that local intramural **drug** infusion does not create new, or worsen existing, dissections produced during standard **balloon angioplasty** in diseased vessels. (C) 1994 Wiley-Liss, Inc.

Descriptors--Author Keywords: **ANGIOPLASTY ; RESTENOSIS ;** INFUSION **BALLOON**

Identifiers--KeyWords Plus: **CORONARY ANGIOPLASTY ; RESTENOSIS ; CATHETER;** MORPHOLOGY; **ARTERIES;** MODEL

Research Fronts: 92-1223 003 (**CORONARY ANGIOPLASTY ; INTRAVASCULAR** ULTRASOUND; ANGIOGRAPHIC **RESTENOSIS**)

Cited References:

BLOCK PC, 1981, V305, P382, NEW ENGL J MED
BREDLAU CE, 1985, V72, P1044, CIRCULATION
CALIFF RM, 1991, V17, P2002, J AM COLL CARDIOL
CERCEK B, 1991, V68, C24, AM J CARDIOL
GAL D, 1990, V119, P291, AM HEART J
GOLDMAN B, 1987, V65, P215, ATHEROSCLEROSIS
HIRSHFELD JW, 1991, V18, P647, J AM COLL CARDIOL
HOLMES DR, 1984, V53, C77, AM J CARDIOL
KUNTZ RE, 1992, V19, P1493, J AM COLL CARDIOL
KUNTZ RE, 1992, V19, P1493, NEW ENGL J MED
LYON RT, 1987, V7, P306, ARTERIOSCLEROSIS
MULLER DWM, 1992, V20, P460, J AM COLL CARDIOL
STADIUS ML, 1993, V126, P47, AM HEART J
TOPOL EJ, 1993, V329, P221, NEW ENGL J MED
WOLINSKY H, 1990, V15, P475, J AM COLL CARDIOL

Title: LOCAL INTRAMURAL DRUG **-DELIVERY USING AN INFUSION** BALLOON **FOLLOWING** ANGIOPLASTY **IN NORMAL AND ATHEROSCLEROTIC VESSELS , 1994**

Abstract: Local intramural delivery of various pharmacologic agents following **angioplasty** has been proposed as a means of reducing **restenosis** . This study tested whether local intramural delivery of aqueous solutions using an infusion **balloon** could be accomplished safely in normal vessels and whether such infusion was safe following standard **angioplasty** in diseased vessels. Infusion of aqueous agents into normal canine **arteries** had no adverse effect. Infusion of several aqueous agents (less-than-or-equal-to 4 **cc** at 4 atm) into diseased swine iliac **arteries** following **balloon angioplasty** did not worsen existing or create new dissections. Histologically, infusion treated vessels did not differ in either model from vessels treated with **angioplasty** alone. We conclude that local intramural **drug** infusion does not create new, or worsen existing, dissections produced during standard **balloon angioplasty** in diseased vessels. (C) 1994 Wiley-Liss, Inc.

...Identifiers-- **CORONARY ANGIOPLASTY ; RESTENOSIS ; CATHETER;** MORPHOLOGY; **ARTERIES;** MODEL

Research Fronts: 92-1223 003 (**CORONARY ANGIOPLASTY ; INTRAVASCULAR** ULTRASOUND; ANGIOGRAPHIC **RESTENOSIS**)

36/5,K/23 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11003276 97356588 PMID: 9213024

Treatment of thrombotic **saphenous** vein **bypass grafts using local urokinase infusion therapy with the Dispatch** catheter .

Glazier J J; Kiernan F J; Bauer H H; Fram D B; Primiano C A; Mitchel J F; Dougherty J E; McKay R G

Department of Internal Medicine, Hartford Hospital, University of Connecticut 06102, USA.

Catheterization and cardiovascular diagnosis (UNITED STATES) Jul **1997** , 41 (3) p261-7, ISSN 0098-6569 Journal Code: 7508512

Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Percutaneous treatment of **thrombotic stenoses** or total **occlusions** in aged saphenous **vein** bypass grafts is associated with a significant incidence of complications primarily related to distal embolization. The purpose of this study was to assess the efficacy of local urokinase delivery with the Dispatch **catheter** prior to **balloon angioplasty** and/or intragraft stent placement as a new technique of **vein** graft revascularization. Local urokinase delivery with the Dispatch **catheter** was performed in 15 saphenous **vein** grafts (mean age = 11.7 +/- 2.5 yr) in 13 patients with unstable or postinfarction angina. The target lesion was a total **occlusion** in 5 of the procedures and a severe **vein** graft **stenosis** in the remaining 10. In all cases, urokinase was administered directly to the site of the **stenosis** / **occlusion** via the Dispatch **catheter** at 0.5 **cc** /min and at a concentration of 30,000 units/ **cc** . The mean urokinase infusion time for the 15 procedures was 33 +/- 10 min (range = 10-60 min) and the mean urokinase dose was 495,000 +/- 158,000 units (range = 150,000-900,000 units). Following Dispatch therapy, mean minimal **lumen** diameter increased from 0.34 +/- 0.32 to 1.81 +/- 0.78 mm ($P < 0.01$), mean TIMI flow increased from 1.9 +/- 1.4 to 2.8 +/- 0.8 ($P < 0.06$), and mean **thrombus** score was reduced from 2.3 +/- 0.6 to 0.3 +/- 0.8 ($P < 0.01$). Mild no- reflow was noted in two cases, although no patient demonstrated angiographic evidence of gross distal embolization. One of the patients with no reflow also demonstrated a small increase in cardiac enzymes. Subsequent **balloon angioplasty** /stent placement was successful in 14 of the 15 procedures (93% success rate). This preliminary report suggests that pretreatment of **thrombotic** saphenous **vein** graft **stenoses** with local urokinase delivery via the Dispatch **catheter** may decrease intragraft **thrombus** and possibly decrease the incidence of **vascular** complications associated with percutaneous intervention. This technique may allow for recanalization of totally **occluded vein** grafts with large clot burdens by using significantly less urokinase and shorter **drug administration** times than conventional **infusion** protocols.

Tags: Comparative Study; Female; Human; Male

Descriptors: **Angioplasty** , Transluminal, Percutaneous **Coronary** --instrumentation--IS; * **Coronary Artery** Bypass; * **Coronary** Disease --surgery--SU; * **Drug** Delivery Systems--instrumentation--IS; *Fibrinolytic Agents-- **administration** and dosage--AD; *Graft **Occlusion** , **Vascular** --drug therapy--DT; * **Thrombolytic** Therapy--instrumentation--IS; *Urinary Plasminogen Activator-- **administration** and dosage--AD; * **Veins** --transplantation--TR; Adult; Aged; **Coronary** Angiography; **Coronary** Disease--radiography--RA; Equipment Design; Graft **Occlusion** , **Vascular** --radiography--RA; Middle Age; Recurrence; Retreatment; Stents; Treatment Outcome

CAS Registry No.: 0 (Fibrinolytic Agents)
Enzyme No.: EC 3.4.21.73 (Urinary Plasminogen Activator)
Record Date Created: 19970821
Record Date Completed: 19970821

Treatment of thrombotic **saphenous** vein **bypass grafts using local urokinase infusion therapy with the Dispatch** catheter .

Jul **1997** ,

Percutaneous treatment of **thrombotic stenoses** or total **occlusions** in aged saphenous **vein** bypass grafts is associated with a significant incidence of complications primarily related to distal embolization...

... of this study was to assess the efficacy of local urokinase delivery with the Dispatch **catheter** prior to **balloon angioplasty** and/or intragraft stent placement as a new technique of **vein** graft revascularization. Local urokinase delivery with the Dispatch **catheter** was performed in 15 saphenous **vein** grafts (mean age = 11.7 +/- 2.5 yr) in 13 patients with unstable or postinfarction angina. The target lesion was a total **occlusion** in 5 of the procedures and a severe **vein** graft **stenosis** in the remaining 10. In all cases, urokinase was administered directly to the site of the **stenosis** / **occlusion** via the Dispatch **catheter** at 0.5 **cc** /min and at a concentration of 30,000 units/ **cc** . The

mean urokinase infusion time for the 15 procedures was 33 +/- 10 min (range = 10...

... 000 +/- 158,000 units (range = 150,000-900,000 units). Following Dispatch therapy, mean minimal **lumen** diameter increased from 0.34 +/- 0.32 to 1.81 +/- 0.78 mm (P < 0...

...from 1.9 +/- 1.4 to 2.8 +/- 0.8 (P < 0.06), and mean **thrombus** score was reduced from 2.3 +/- 0.6 to 0.3 +/- 0.8 (P < 0...
... of the patients with no reflow also demonstrated a small increase in cardiac enzymes. Subsequent **balloon angioplasty** /stent placement was successful in 14 of the 15 procedures (93% success rate). This preliminary report suggests that pretreatment of **thrombotic** saphenous **vein** graft **stenoses** with local urokinase delivery via the Dispatch **catheter** may decrease intragraft **thrombus** and possibly decrease the incidence of **vascular** complications associated with percutaneous intervention. This technique may allow for recanalization of totally **occluded vein** grafts with large clot burdens by using significantly less urokinase and shorter **drug administration** times than conventional **infusion** protocols.
Descriptors: **Angioplasty** , Transluminal, Percutaneous **Coronary** --instrumentation--IS; * **Coronary Artery** Bypass; * **Coronary** Disease --surgery--SU; * **Drug** Delivery Systems--instrumentation--IS; *Fibrinolytic Agents-- **administration** and dosage--AD; *Graft **Occlusion** , **Vascular** --drug therapy--DT; * **Thrombolytic** Therapy--instrumentation--IS; *Urinary Plasminogen Activator-- **administration** and dosage--AD; * **Veins** --transplantation--TR; Adult; Aged; **Coronary** Angiography; **Coronary** Disease--radiography--RA; Equipment Design; Graft **Occlusion** , **Vascular** --radiography--RA; Middle Age; Recurrence; Retreatment; Stents; Treatment Outcome

36/5,K/28 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07544981 92901505 PMID: 10149895
Anticoagulant **effect of iohexol vs. ioxaglate during cardiac** catheterization .
Vacek J L; Hibiya K; Rosamond T L; Kramer P H; Crouse L J; Robuck W; Beauchamp G D
Mid America Heart Institute, St. Luke's Hospital, Kansas City, Missouri.
Journal of invasive cardiology (UNITED STATES) Apr **1992** , 4 (3) p139-44, ISSN 1042-3931 Journal Code: 8917477
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: HEALTH TECHNOLOGY ASSESSMENT
Contrast agent safety during cardiac **catheterization** (**CC**) may relate in part to anti- or procoagulant effect. We studied these effects in 177 patients who underwent standard **CC** (N=112) or percutaneous transluminal **coronary angioplasty** (PTCA) (N=65) and received either iohexol (N=111) or ioxaglate (N=66). Patients received either 0 or 2000u heparin for **CC** or 10,000u for PTCA. The groups were similar in regards to age, sex, amount of contrast used, and procedure time. Partial **thromboplastin** time (PTT) and activated clotting time (ACT) were both significantly increased (P less than .01) in patients who received 10,000u heparin irrespective of type of contrast agent although larger increases were seen in the iohexol group. With 2000u of heparin, ACT and PTT increased significantly (P less than .01) only in the iohexol group. PTT and ACT actually decreased to similar and significant (P less than .01) degrees after both iohexol and ioxaglate when heparin was not used. We conclude: 1) commonly used measures of **anticoagulant** (ACT and PTT) show greater prolongation after either 2000 or 10,000u of heparin with iohexol than ioxaglate, 2) ACT and PCT appear to shorten with both iohexol and ioxaglate if no heparin is used. This data would suggest that ioxaglate does not have an **anticoagulant** advantage over iohexol.
Tags: Comparative Study; Human; Male

Descriptors: **Anticoagulants** --pharmacology--PD; *Heart **Catheterization** ; *Iohexol--pharmacology--PD; *Ioxaglic Acid--pharmacology--PD; Aged; **Angioplasty** , Transluminal, Percutaneous **Coronary** ; Heparin --administration and dosage--AD; Middle Age; Partial **Thromboplastin** Time; Prospective Studies; Whole Blood Coagulation Time

CAS Registry No.: 0 (Anticoagulants); 59017-64-0 (Ioxaglic Acid); 66108-95-0 (Iohexol); 9005-49-6 (Heparin)

Record Date Created: 19920827

Record Date Completed: 19920827

Anticoagulant **effect of iohexol vs. ioxaglate during cardiac** catheterization .

Apr **1992** ,

Contrast agent safety during cardiac **catheterization** (**CC**) may relate in part to anti- or procoagulant effect. We studied these effects in 177 patients who underwent standard **CC** (N=112) or percutaneous transluminal **coronary angioplasty** (PTCA) (N=65) and received either iohexol (N=111) or ioxaglate (N=66). Patients received either 0 or 2000u heparin for **CC** or 10,000u for PTCA. The groups were similar in regards to age, sex, amount of contrast used, and procedure time. Partial **thromboplastin** time (PTT) and activated clotting time (ACT) were both significantly increased (P less than .01...

... iohexol and ioxaglate when heparin was not used. We conclude: 1) commonly used measures of **anticoagulant** (ACT and PTT) show greater prolongation after either 2000 or 10,000u of heparin with...

... if no heparin is used. This data would suggest that ioxaglate does not have an **anticoagulant** advantage over iohexol.

Descriptors: **Anticoagulants** --pharmacology--PD; *Heart **Catheterization** ; *Iohexol--pharmacology--PD; *Ioxaglic Acid--pharmacology--PD; Aged; **Angioplasty** , Transluminal, Percutaneous **Coronary** ; Heparin --administration and dosage--AD; Middle Age; Partial **Thromboplastin** Time; Prospective Studies; Whole Blood Coagulation Time

Chemical Name: **Anticoagulants** ; Ioxaglic Acid; Iohexol; Heparin

36/5,K/32 (Item 11 from file: 155)

07300371 92163303 PMID: 1983582

Systemic lysis in subacute arterial occlusion]

Systemische Lyse bei subakuten **Arterienverschlussen** .

Martin M; Fiebach B J

Geriatrische Klinik, Stadtische Kliniken, Duisburg.

Langenbecks Archiv fur Chirurgie. Supplement II, Verhandlungen der Deutschen Gesellschaft fur Chirurgie. Deutsche Gesellschaft fur Chirurgie. Kongress (GERMANY) **1990** , p417-20, ISSN 0173-0541 Journal Code: 9200455

Document type: Journal Article ; English Abstract

Languages: GERMAN

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The therapeutic regimen used consisted of an ultrahigh streptokinase dosage scheme with an **infusion rate** of 1.5 million units per hour over a period of 6 hours. Where no immediate clearance occurred or where residual **stenoses** persisted, a **catheter** dilation (PTA) was subsequently carried out. Favorable results were achieved in the group of up to 6 week old femoral **occlusions** with 2 or 3 calf **arteries** open and an **occlusion** length below 15 cm. Iliac **occlusions** responded well to lytic treatment if a 3 month history was not exceeded.

Tags: Human

Descriptors: **Arterial Occlusive** Diseases-- **drug** therapy--DT; * **Ischemia** -- **drug therapy** --DT; *Leg--blood supply--BS; *Streptokinase --administration and dosage--AD; * **Thrombolytic** Therapy--methods--MT; **Angioplasty , Balloon ; Arterial Occlusive** Diseases--radiography--RA; Combined Modality Therapy; Dose-Response Relationship, **Drug** ; **Drug**

Administration Schedule; Infusions, **Intravenous** ; **Ischemia** --radiography --RA
Enzyme No.: EC 3.4.- (Streptokinase)
Record Date Created: 19920331
Record Date Completed: 19920331

Systemic lysis in subacute arterial occlusion]
Systemische Lyse bei subakuten **Arterienverschlussen** .
1990 ,
The therapeutic regimen used consisted of an ultrahigh streptokinase dosage scheme with an **infusion rate** of 1.5 million units per hour over a period of 6 hours. Where no immediate clearance occurred or where residual **stenoses** persisted, a **catheter** dilation (PTA) was subsequently carried out. Favorable results were achieved in the group of up to 6 week old femoral **occlusions** with 2 or 3 calf **arteries** open and an **occlusion** length below 15 cm. Iliac **occlusions** responded well to lytic treatment if a 3 month history was not exceeded.
Descriptors: **Arterial Occlusive** Diseases-- **drug** therapy--DT; * **Ischemia -- drug therapy** --DT; *Leg--blood supply--BS; *Streptokinase --administration and dosage--AD; * **Thrombolytic** Therapy--methods--MT; **Angioplasty , Balloon ; Arterial Occlusive** Diseases--radiography--RA; Combined Modality Therapy; Dose-Response Relationship, **Drug ; Drug** Administration Schedule; Infusions, **Intravenous** ; **Ischemia** --radiography --RA

36/5,K/37 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06331160 89347441 PMID: 2763230
Differential lung function in an infant with the Swyer-James syndrome.
Avital A; Shulman D L; Bar-Yishay E; Noviski N; Schachter J; Krausz Y; Godfrey S
Pulmonary Function Laboratory, Hadassah University Hospital, Jerusalem, Israel.
Thorax (ENGLAND) Apr **1989** , 44 (4) p298-302, ISSN 0040-6376 Journal Code: 0417353
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
A previously healthy two year old boy had an adenoviral infection at the age of 13 months and developed hyperlucency of the left lung, chronic respiratory distress, and failure to thrive. Bronchodilators and steroid treatment had no effect. **Radionuclide** lung scans using an **intravenous** bolus of xenon-133 both before and after treatment showed substantially reduced function on the hyperlucent side and modestly reduced function on the other side. Fibreoptic bronchoscopy showed no structural abnormalities. Partial forced expiratory flow volume (PEFV) curves, generated from end inspiration by rapid compression of the chest wall with an **inflatable** jacket, were obtained from the total respiratory system and from each lung separately by **inflating** a Fogarty **catheter** in the contralateral mainstem bronchus. Expiratory **flow rates** and volumes during both tidal breathing and PEFV manoeuvres were considerably decreased in the hyperlucent lung. PEFV curves from the "healthy" right lung and from the total respiratory system were similar in shape and showed a moderately **obstructive** pattern. The right lung ventilated about four times as much as the left when measured by bronchospirometry and about three times as much when measured by the **radionuclide** technique. The lung scans appeared to reflect adequately the functional abnormality in this infant with the Swyer-James syndrome.
Tags: Case Report; Human; Male
Descriptors: Lung--physiopathology--PP; *Lung Diseases, **Obstructive** --physiopathology--PP; Child, Preschool; Lung-- **radionuclide** imaging--RI; Lung Diseases, **Obstructive** -- **radionuclide** imaging--RI; Respiratory Function Tests; Syndrome; Xenon **Radioisotopes** --diagnostic use--DU

CAS Registry No.: 0 (Xenon Radioisotopes)
Record Date Created: 19890908
Record Date Completed: 19890908

Apr **1989** ,
... lung, chronic respiratory distress, and failure to thrive. Bronchodilators and steroid treatment had no effect. **Radionuclide** lung scans using an **intravenous** bolus of xenon-133 both before and after treatment showed substantially reduced function on the...

...PEFV) curves, generated from end inspiration by rapid compression of the chest wall with an **inflatable** jacket, were obtained from the total respiratory system and from each lung separately by **inflating** a Fogarty **catheter** in the contralateral mainstem bronchus. Expiratory **flow rates** and volumes during both tidal breathing and PEFV manoeuvres were considerably decreased in the hyperlucent...

... lung and from the total respiratory system were similar in shape and showed a moderately **obstructive** pattern. The right lung ventilated about four times as much as the left when measured by bronchospirometry and about three times as much when measured by the **radionuclide** technique. The lung scans appeared to reflect adequately the functional abnormality in this infant with...
Descriptors: Lung--physiopathology--PP; *Lung Diseases, **Obstructive** --physiopathology--PP; Child, Preschool; Lung-- **radionuclide** imaging--RI; Lung Diseases, **Obstructive** -- **radionuclide** imaging--RI; Respiratory Function Tests; Syndrome; Xenon **Radioisotopes** --diagnostic use--DU
Chemical Name: Xenon **Radioisotopes**

36/5,K/39 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05575258 87254485 PMID: 3599210
The effect of papaverine on arterial **and** venous **hemodynamics of erection.**
Delcour C; Wespes E; Vandenbosch G; Schulman C C; Struyven J
Journal of urology (UNITED STATES) Jul **1987** , 138 (1) p187-9, ISSN 0022-5347 Journal Code: 0376374
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS
The aim of this study was to establish how much of the erectogenic effect of papaverine is due to **arterial** dilatation and how much to **venous** **obstruction** during artificial erection. Three consecutive cavernosographies were done on each of 10 psychogenic impotent patients: a baseline run without papaverine; a run with papaverine (60 mg. intracavernously) after **occlusion** of **arterial** supply to the corpora cavernosa with **balloon** **catheters** **inflated** at the origin of the hypogastric **arteries** ; and a third run after restoring **arterial** blood supply to the corpora. The measured **flow rates** indicated that during cavernosography in papaverine-induced erection, the major effect of papaverine is to increase the resistance to **venous** outflow from the corpora cavernosa.
Tags: Human; Male
Descriptors: Papaverine--pharmacology--PD; *Penile Erection-- **drug** effects--DE; *Penis--blood supply--BS; Adult; Hemodynamics-- **drug** effects --DE; Impotence--diagnosis--DI; Middle Age; Regional Blood Flow-- **drug** effects--DE; **Vascular** Resistance-- **drug** effects--DE
CAS Registry No.: 58-74-2 (Papaverine)
Record Date Created: 19870727
Record Date Completed: 19870727

The effect of papaverine on arterial **and** venous **hemodynamics of erection.**

Jul **1987** ,

... study was to establish how much of the erectogenic effect of papaverine is due to **arterial** dilatation and how much to **venous** **obstruction** during artificial erection. Three consecutive cavernosographies were done on each of 10 psychogenic impotent patients: a baseline run without papaverine; a run with papaverine (60 mg. intracavernously) after **occlusion** of **arterial** supply to the corpora cavernosa with **balloon** **catheters** **inflated** at the origin of the hypogastric **arteries** ; and a third run after restoring **arterial** blood supply to the corpora. The measured **flow** **rates** indicated that during cavernosography in papaverine-induced erection, the major effect of papaverine is to increase the resistance to **venous** outflow from the corpora cavernosa.

Descriptors: Papaverine--pharmacology--PD; *Penile Erection-- **drug** effects--DE; *Penis--blood supply--BS; Adult; Hemodynamics-- **drug** effects --DE; Impotence--diagnosis--DI; Middle Age; Regional Blood Flow-- **drug** effects--DE; **Vascular** Resistance-- **drug** effects--DE

36/5,K/45 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03592395 82002858 PMID: 122266

Nitroglycerin in acute myocardial infarction. X. Effect of small and large doses of nitroglycerin on sigma ST segment deviation -- experimental and clinical results.

Bussmann W D; Schofer H; Kurita A; Ganz W

Clinical cardiology (UNITED STATES) Apr **1979** , 2 (2) p106-12, ISSN 0160-9289 Journal Code: 7903272

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The purpose of the present study was to investigate the effect of the dose of nitroglycerin (NTG) on myocardial **ischemic** injury. In 20 closed chest dogs the anterior descending branch of the left **coronary** **artery** was **occluded** by **inflating** a **balloon** in its **lumen** . Compared with the untreated control group the sigma ST elevation was significantly lower when NTG was applied at a rate of 0.02 mg/min, but significantly higher when NTG was administered at a rate of 0.10 mg/min. In 12 patients with acute myocardial infarction NTG was infused at a rate of 3 mg in the first hour (0.05 mg/min) and 6 mg in the second hour (0.1 mg/min). Sigma ST elevation and sigma ST depression decreased during the lower **infusion** **rate** (p less than 0.001). When the rate of NTG infusion was raised to 6 mg/hr, the improvement in ST segment deviation was partially reversed. This effect, particularly evident in patients not in heart failure, was associated with a significant rise in heart rate (p less than 0.05) and a fall in diastolic **arterial** pressure (p less than 0.025). Patients with left ventricular failure were less sensitive to higher doses of NTG than those without failure. Thus, the effect of NTG on myocardial **ischemic** injury depends on the NTG dose and on the functional state of the injured left ventricle.

Tags: Animal; Female; Human; Male

Descriptors: Electrocardiography; *Myocardial Infarction-- **drug** therapy --DT; *Nitroglycerin--administration and dosage--AD; Dogs; Heart Ventricle --physiopathology--PP; Hemodynamics-- **drug** effects--DE; Myocardial Infarction--pathology--PA; Myocardial Infarction--physiopathology--PP; Nitroglycerin--pharmacology--PD

CAS Registry No.: 55-63-0 (Nitroglycerin)

Record Date Created: 19811122

Record Date Completed: 19811122

Apr **1979** ,

... present study was to investigate the effect of the dose of nitroglycerin (NTG) on myocardial **ischemic** injury. In 20 closed chest dogs the anterior descending branch of the left **coronary** **artery** was

occluded by **inflating** a **balloon** in its **lumen** . Compared with the untreated control group the sigma ST elevation was significantly lower when NTG...

...0.1 mg/min). Sigma ST elevation and sigma ST depression decreased during the lower **infusion rate** (p less than 0.001). When the rate of NTG infusion was raised to 6...

... significant rise in heart rate (p less than 0.05) and a fall in diastolic **arterial** pressure (p less than 0.025). Patients with left ventricular failure were less sensitive to higher doses of NTG than those without failure. Thus, the effect of NTG on myocardial **ischemic** injury depends on the NTG dose and on the functional state of the injured left...
Descriptors: Electrocardiography; *Myocardial Infarction-- **drug** therapy --DT; *Nitroglycerin--administration and dosage--AD; Dogs; Heart Ventricle --physiopathology--PP; Hemodynamics-- **drug** effects--DE; Myocardial Infarction--pathology--PA; Myocardial Infarction--physiopathology--PP; Nitroglycerin--pharmacology--PD

36/5,K/49 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06917515 EMBASE No: 1997201960
Treatment of thrombotic **saphenous** vein **bypass grafts using local urokinase infusion therapy with the dispatch** catheter
Glazier J.J.; Kiernan F.J.; Bauer H.H.; Fram D.B.; Primiano C.A.; Mitchel J.F.; Dougherty J.E.; McKay R.G.
Dr. R.G. McKay, Cardiac Laboratory, Hartford Hospital, 80 Seymour Street, Hartford, CT 06102 United States
Catheterization and Cardiovascular Diagnosis (CATHETER. CARDIOVASC. DIAGN.) (United States) 1997, 41/3 (261-267)
CODEN: CCDID ISSN: 0098-6569
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 13

Percutaneous treatment of **thrombotic stenoses** or total **occlusions** in aged saphenous **vein** bypass grafts is associated with a significant incidence of complications primarily related to distal embolization. The purpose of this study was to assess the efficacy of local urokinase delivery with the Dispatch **catheter** prior to **balloon angioplasty** and/or intragraft stent placement as a new technique of **vein** graft revascularization. Local urokinase delivery with the Dispatch **catheter** was performed in 15 saphenous **vein** grafts (mean age = 11.7 +/- 2.5 yr) in 13 patients with unstable or postinfarction angina. The target lesion was a total **occlusion** in 5 of the procedures and a severe **vein** graft **stenosis** in the remaining 10. In all cases, urokinase was administered directly to the site of the **stenosis / occlusion** via the Dispatch **catheter** at 0.5 **cc** /min end at a concentration of 30,000 units/ **cc** . The mean urokinase infusion time for the 15 procedures was 33 +/- 10 min (range = 10- 60 min) and the mean urokinase dose was 495,000 +/- 158,000 units (range = 150,000-900,000 units). Following Dispatch therapy, mean minimal **lumen** diameter increased from 0.34 +/- 0.32 to 1.81 +/- 0.78 mm (P < 0.01), mean TIMI flow increased from 1.9 +/- 1.4 to 2.8 +/- 0.8 (P <: 0.06), and mean **thrombus** score was reduced from 2.3 +/- 0.6 to 0.3 +/- 0.8 (P<: 0.01). Mild no reflow was noted in two cases, although no patient demonstrated angiographic evidence of gross distal embolization. One of the patients with no reflow also demonstrated a small increase in cardiac enzymes. Subsequent **balloon angioplasty** /stent placement was successful in 14 of the 15 procedures (93% success rate). This preliminary report suggests that pretreatment of **thrombotic** saphenous **vein** graft **stenoses** with local urokinase delivery via the Dispatch **catheter** may decrease intragraft **thrombus** and possibly decrease the incidence of **vascular** complications associated with percutaneous intervention. This technique may allow for recanalization of totally **occluded vein** grafts with large clot burdens by using significantly less urokinase and shorter **drug**

administration times than conventional **infusion** protocols.

BRAND NAME/MANUFACTURER NAME: abbokinase/abbott; persantine; nitroglycerin; aspirin; coumadin
MANUFACTURER NAMES: abbott
DRUG DESCRIPTORS:
*urokinase-- **drug** **administration** --ad; *urokinase-- **drug** therapy--dt acetylsalicylic acid; beta adrenergic receptor blocking agent; calcium channel blocking agent; dipyridamole; glyceryl trinitrate; heparin; plasminogen activator; verapamil; warfarin
MEDICAL DESCRIPTORS:
*angina pectoris--surgery--su; *bypass surgery; *graft **occlusion** --complication--co; *graft **occlusion** --drug therapy--dt; *saphenous **vein** graft; * **thrombosis** --complication--co; * **thrombosis** -- **drug therapy** --dt adult; aged; angiography; article; artificial embolism; **balloon** **catheter** ; clinical article; clinical protocol; controlled study; **drug** **infusion** ; female; fibrinolytic therapy; guide wire; human; human tissue; **intravenous** **drug** **administration** ; male; percutaneous transluminal **angioplasty** ; revascularization; stent
CAS REGISTRY NO.: 139639-24-0 (urokinase); 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1 (acetylsalicylic acid); 58-32-2 (dipyridamole); 55-63-0 (glyceryl trinitrate); 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5 (heparin); 9039-53-6 (plasminogen activator); 152-11-4, 52-53-9 (verapamil); 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2 (warfarin)
SECTION HEADINGS:
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
037 **Drug** Literature Index

Treatment of thrombotic **saphenous** vein **bypass grafts using local urokinase infusion therapy with the dispatch** catheter

Percutaneous treatment of **thrombotic** **stenoses** or total **occlusions** in aged saphenous **vein** bypass grafts is associated with a significant incidence of complications primarily related to distal embolization...

...of this study was to assess the efficacy of local urokinase delivery with the Dispatch **catheter** prior to **balloon** **angioplasty** and/or intragraft stent placement as a new technique of **vein** graft revascularization. Local urokinase delivery with the Dispatch **catheter** was performed in 15 saphenous **vein** grafts (mean age = 11.7 +/- 2.5 yr) in 13 patients with unstable or postinfarction angina. The target lesion was a total **occlusion** in 5 of the procedures and a severe **vein** graft **stenosis** in the remaining 10. In all cases, urokinase was administered directly to the site of the **stenosis** / **occlusion** via the Dispatch **catheter** at 0.5 **cc** /min end at a concentration of 30,000 units/ **cc** . The mean urokinase infusion time for the 15 procedures was 33 +/- 10 min (range = 10...

...000 +/- 158,000 units (range = 150,000-900,000 units). Following Dispatch therapy, mean minimal **lumen** diameter increased from 0.34 +/- 0.32 to 1.81 +/- 0.78 mm (P < 0...

...from 1.9 +/- 1.4 to 2.8 +/- 0.8 (P <: 0.06), and mean **thrombus** score was reduced from 2.3 +/- 0.6 to 0.3 +/- 0.8 (P<: 0...

...of the patients with no reflow also demonstrated a small increase in cardiac enzymes. Subsequent **balloon** **angioplasty** /stent placement was successful in 14 of the 15 procedures (93% success rate). This preliminary report suggests that pretreatment of **thrombotic** saphenous **vein** graft **stenoses** with local urokinase delivery via the Dispatch **catheter** may decrease intragraft **thrombus** and possibly decrease the incidence of **vascular** complications associated with percutaneous intervention. This technique may allow for recanalization of totally **occluded** **vein** grafts with large clot burdens by using significantly less urokinase and shorter **drug** **administration** times than conventional **infusion** protocols.

DRUG DESCRIPTORS:
*urokinase-- **drug** **administration** --ad; *urokinase-- **drug** therapy--dt
MEDICAL DESCRIPTORS:
*angina pectoris--surgery--su; *bypass surgery; *graft **occlusion** --complication--co; *graft **occlusion** --drug therapy--dt; *saphenous **vein** graft; * **thrombosis** --complication--co; * **thrombosis** -- **drug therapy** --dt adult; aged; angiography; article; artificial embolism; **balloon** **catheter** ; clinical article; clinical protocol; controlled study; **drug** **infusion** ; female; fibrinolytic therapy; guide wire; human; human tissue; **intravenous** **drug** **administration** ; male; percutaneous transluminal **angioplasty** ; revascularization; stent
SECTION HEADINGS:
...Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
027 Biophysics, Bioengineering and Medical Instrumentation
037 **Drug** Literature Index
1997
?

```
Set     Items   Description
S1     175992   (VENOUS OR VEIN? OR ARTERY OR ARTERI? OR VASCULAR? OR INTR-
             ?VASC? OR INTR?VEN? OR BLOOD?()VESSEL? OR VENAL OR CORONAR?)
S2      78229   OCCLUD? OR OCCLUSI? OR OBSTRUCT? OR STENOS? OR STENOT? OR -
             RESTENOS? OR RESTENOT? OR PLAQUE?
S3      66259   SCLERO? OR THROMB? OR BLOODCLOT? OR BLOOD()CLOT? OR ISCHEM-
             I? OR ARTER?SCLER? OR PLAQUING
S4        367   CALCIUM()DEPOSIT?
S5     340080   BALLOON? OR PLASTY? OR PLASTIE? ? OR ANGIOPLAST? OR OCCLU?-
             ()DEVICE? OR INFLAT? OR CARDIOPLAST?
S6          1   ARTERIOPLAST?
S7    4824648   DELIVER? OR ADMINIST? OR INJECT? OR INFUS? OR PERFUS?
S8      43377   CATHETER? OR CANNULA? OR CANULA? OR TROCAR? OR LUMEN? OR H-
             OLLOW?(N)WIRE?
S9    1199591   DRUG? OR NARCOTIC? OR OCCLU?(N)TREAT? OR ANTICOAGUL? OR AN-
             TI()COAGUL? OR THROMBYT?
S10     8178   RADIONUCLID? OR RADIO()NUCLID? OR RADIOISOTOP? OR RADIO()I-
             SOTOP? OR RADIOACTIVE()ISOTOP?
S11        6   RADIO()ACTIVE()ISOTOP?
S12    95165   FLOWRATE? OR FLOW()RATE? OR "CC" OR "C.C." OR CUBIC()CENTI-
             L?
S13   238441   S7(10N)(S9 OR S10 OR S11)
S14      214   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6) AND S8 AND S12
S15       71   S13 AND S14
S16    75218   S3 OR ARTERI?SCLER? OR ARTER?()SCLER? OR ARTHER?SCLER? OR -
             ARTHER?()SCLER? OR ATHER?SCLER? OR ATHER?()SCLER?
S17   340117   S5 OR (CARDIO? OR ANGIO?)()PLAST?
S18  1200917   S9 OR THROMBOL?
S19    95709   S12 OR (INFUS? OR PERFUS?)()RATE?
S20   238893   S7(10N)(S9 OR S10 OR S11 OR S18)
S21      242   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6 OR S17) AND S8 AND (-
             S12 OR S19)
S22       99   S20 AND S21
S23    25838   S1(10N)(S2 OR S3 OR S4)
S24   340118   S5 OR S6 OR S17
S25   238893   S7(10N)(S9 OR S10 OR S11 OR S18)
S26      164   S8(10N)(S12 OR S19)
S27        4   S23 AND S24 AND S25 AND S26
S28        2   S27 AND PY<1999
S29    22480   1(S)(S2 OR S3 OR S4)
S30    22107   29 AND S25
S31    52617   7(S)(S9 OR S10 OR S11 OR S18)
S32    20121   30 AND S31
S33      965   S9(S)(S12 OR S19)
S34     2979   S29 AND S31
S35      235   S31 AND S33
S36   718134   35 AND PY<1999
S37      193   S35 AND PY<1999
S38      118   S37 AND S20
S39       68   S22 AND PY<1999
?show files
File  16:Gale Group PROMT(R) 1990-2003/Sep 26
         (c) 2003 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2003/Sep 29
         (c)2003 The Gale Group
File 621:Gale Group New Prod.Annou.(R) 1985-2003/Sep 29
         (c) 2003 The Gale Group
File 444:New England Journal of Med. 1985-2003/Sep W4
         (c) 2003 Mass. Med. Soc.
?
```

39/5,K/3 (Item 3 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)

05502178 Supplier Number: 48337153 (USE FORMAT 7 FOR FULLTEXT)
InterVentional Technologies Announces Successful Completion of FullFlow Perfusion Dilation Catheter **Trials.**
Business Wire, p03050349
March 5, 1998
Language: English Record Type: Fulltext
Document Type: Newswire; Trade
Word Count: 296
PUBLISHER NAME: Business Wire
COMPANY NAMES: *InterVentional Technologies Inc.
EVENT NAMES: *331 (Product development)
GEOGRAPHIC NAMES: *1USA (United States)
PRODUCT NAMES: 3842240 (**Angioplasty** Supplies)
INDUSTRY NAMES: BUS (Business, General); BUSN (Any type of business)
NAICS CODES: 339113 (Surgical Appliance and Supplies Manufacturing)
SPECIAL FEATURES: COMPANY

(USE FORMAT 7 FOR FULLTEXT)
InterVentional Technologies Announces Successful Completion of FullFlow Perfusion Dilation Catheter **Trials.**
TEXT:
...the successful completion of an extensive series of animal trials of the FullFlow perfusion dilation **catheter** .
... Washington, D.C. They conclusively demonstrate the device's capability to effectively and safely dilate **coronary arteries** while allowing near normal physiologic blood- **flow rates** throughout the procedure.
The FullFlow perfusion dilation **catheter** replaces the traditional **angioplasty balloon** with a retracting spring mesh. When deployed in the vessel, this mesh forms a scaffold...

...for blood flow, while at the same time providing significant radial dilating force. This new **catheter** facilitates prolonged vessel dilation without risk of **ischemia** or infarction.
Commenting on Segal's results, Rob Michiels, InterVentional Technologies' president and chief operating officer, noted: "Not only does this over-the-wire **catheter** allow more than three times the blood flow of currently marketed perfusion dilation **balloons** , it also permits side-branch perfusion and eliminates the need for a **balloon inflation** /deflation device.
"This is a significant breakthrough for high-risk patients receiving **angioplasty** treatment."
The company is assembling these data into an appropriate regulatory submission and plans to...

...San Diego; Murietta, Calif.; and Letterkenny, Ireland.
The company manufactures and markets worldwide, the TEC **thrombectomy catheter** , the Cutting **Balloon** microsurgical dilation **catheter** , the TRACKWIRE family of guide wires, the LP Stent, the INFILTRATOR **arterial** -wall **drug - delivery catheter** and the IRADIATOR **arterial** -wall radiotherapy system (see note). -0-
NOTE TO EDITORS: Some products are investigational use only...
PRODUCT NAMES: 3842240 (**Angioplasty** Supplies)
19980305

39/5,K/6 (Item 6 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)

03614170 Supplier Number: 45090165 (USE FORMAT 7 FOR FULLTEXT)
LOCALMED RECEIVES FDA APPROVAL TO MARKET THE INFUSASLEEVE CORONARY DRUG DELIVERY CATHETER

PR Newswire, pN/A
Oct 26, 1994
Language: English Record Type: Fulltext
Document Type: Newswire; Trade
Word Count: 441
PUBLISHER NAME: PR Newswire Association, Inc.
COMPANY NAMES: *LocalMed
EVENT NAMES: *330 (Product information)
GEOGRAPHIC NAMES: *1U9CA (California); 1USA (United States)
PRODUCT NAMES: 2834030 (**Drug Delivery** Systems); 3842242 (Therapeutic **Balloon Catheters**)
INDUSTRY NAMES: BUS (Business, General); BUSN (Any type of business)
NAICS CODES: 325412 (Pharmaceutical Preparation Manufacturing); 339113 (Surgical Appliance and Supplies Manufacturing)
TRADE NAMES: InfusaSleeve
SPECIAL FEATURES: COMPANY

LOCALMED RECEIVES FDA APPROVAL TO MARKET THE INFUSASLEEVE CORONARY DRUG DELIVERY CATHETER

CORONARY DRUG DELIVERY CATHETER

PALO ALTO, CA., Oct. 26 /PRNewswire/ -- LocalMed, Inc., announced today that it has received FDA approval to market the Kaplan-Simpson InfusaSleeve(TM), a **catheter** which delivers medication directly to the **coronary artery** during **angioplasty** .

With more than a third of the world's 700,000 **angioplasty** patients requiring a second procedure within six months, the quest for a drug that prevents **restenosis** has been the industry's holy grail. Nearly fifty pharmaceutical and biotechnology firms are developing...

...in the hope that they will have some impact on this persistent problem. Available anti- **thrombotic** drugs like heparin, and direct **thrombin** inhibitors now under investigation, could also be very effective in reducing the risk of abrupt vessel closure in **angioplasty** after acute myocardial infarction. In all cases, though, the trick lies in **delivering** the **drug** to the injured segment of the **coronary artery** .

LocalMed believes it has the answer. Using its patented, over-the- **balloon** technology, the Palo Alto company has developed an infusion sleeve which tracks over virtually any **angioplasty balloon** and can deliver medication directly to the **angioplasty** site. The **InfusaSleeve** (TM) uses the existing **balloon** to position its **drug delivery** ports against the **artery** wall, permitting a precise fit within the **artery** and independent control of **drug infusion** , which the company believes is crucial for safe and effective local delivery.

This independent control...

...and clinical studies are any indication, they may be right. "Our preclinical trials demonstrated remarkable **drug delivery** efficiency with almost no injury," said Paul Goeld, LocalMed's CEO, "but our biggest advantages are flexibility and low cost. **Drugs** can be **infused** at virtually any pressure, **flow rate** or volume. It's safe, effective and easy to use." The company is currently planning...

...Frankfurt, Germany and Milan, Italy. The device has been used in combination with most popular **angioplasty balloon catheters** and with three commercially available **coronary** stents. In addition, LocalMed is a collaborative partner in several investigations requiring intramural (**arterial** wall) delivery.

LocalMed is a private, venture-backed company. Its investors include Brentwood Associates, Burr...

PRODUCT NAMES: 2834030 (**Drug Delivery** Systems); 3842242 (Therapeutic **Balloon Catheters**)
19941026

39/5,K/7 (Item 7 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)

01874597 Supplier Number: 42379271
CATHETER **CLEARS** CORONARY ARTERIES
Design News, p88
Sept 23, 1991
ISSN: 0011-9407
Language: English Record Type: Abstract
Document Type: Magazine/Journal; Refereed; Academic Trade

ABSTRACT:
Heart Technology (Bellevue, WA) has developed instrumentation that removes **plaque** deposits from clogged **arteries** . The Rotablator is a pneumatically-powere **angioplasty** system that makes use of a diamond crystal-coated **catheter** tip that erodes **plaque** into particles smaller than red blood cells, eliminating the need for a collection system. The device includes an air- or nitorgen-using power source, a control console, a steerable guide wire 0.009-in in diameter, and an advancer/ **catheter** . Through a small incision in the femoral **artery** the system is inserted and moved to the **plaque** target. Driven by a flexible helical drive shaft, the **catheter** tip rotates at 150,000-rpm to 190,000-rpm. The apparatus also delivers a 10- **cc** /min saline flush. The instrument is said to be able to deal with any type of **plaque** , even hardened deposits, and to cause no damage to elastic tissue, which just moves out of the way of the **catheter** tip. Work on the system was begun in 1981 by David Auth, now chairman of the $100 mil privately held company. Sidebars disclose that the device has received approval from the Federal **Drug Administration** (FDA) for use in clearing of periperal **arteries** , and permission for general use on **coronary arteries** is expected in 1991. Investigative use of the Rotablator for **arteries** of the heart has been in progress since 1988.
PUBLISHER NAME: Cahners Publishing Company
COMPANY NAMES: *Heart Technology Inc.
EVENT NAMES: *330 (Product information)
GEOGRAPHIC NAMES: *1USA (United States)
PRODUCT NAMES: *3841540 (Cardiovascular Therapy Equip)
INDUSTRY NAMES: ARCH (Architecture and Design); BUSN (Any type of business); ELEC (Electronics)
NAICS CODES: 339112 (Surgical and Medical Instrument Manufacturing)
TICKER SYMBOLS: HRTT
SPECIAL FEATURES: COMPANY

CATHETER **CLEARS** CORONARY ARTERIES

ABSTRACT:
Heart Technology (Bellevue, WA) has developed instrumentation that removes **plaque** deposits from clogged **arteries** . The Rotablator is a pneumatically-powere **angioplasty** system that makes use of a diamond crystal-coated **catheter** tip that erodes **plaque** into particles smaller than red blood cells, eliminating the need for a collection system. The...

...a control console, a steerable guide wire 0.009-in in diameter, and an advancer/ **catheter** . Through a small incision in the femoral **artery** the system is inserted and moved to the **plaque** target. Driven by a flexible helical drive shaft, the **catheter** tip rotates at 150,000-rpm to 190,000-rpm. The apparatus also delivers a 10- **cc** /min saline flush. The instrument is said to be able to deal with any type of **plaque** , even hardened deposits, and to cause no damage to elastic tissue, which just moves out of the way of the **catheter** tip. Work on the system was begun in 1981 by David Auth, now chairman of...

...mil privately held company. Sidebars disclose that the device has

received approval from the Federal **Drug Administration** (FDA) for use in clearing of periperal **arteries** , and permission for general use on **coronary arteries** is expected in 1991. Investigative use of the Rotablator for **arteries** of the heart has been in progress since 1988.
...
19910923

39/5,K/12 (Item 5 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

10050578 SUPPLIER NUMBER: 20358089 (USE FORMAT 7 OR 9 FOR FULL TEXT)
InterVentional Technologies Announces Successful Completion of FullFlow Perfusion Dilation Catheter **Trials.**
Business Wire, p3050349
March 5, 1998
LANGUAGE: English RECORD TYPE: Fulltext
WORD COUNT: 323 LINE COUNT: 00033

COMPANY NAMES: InterVentional Technologies Inc.--Product development
INDUSTRY CODES/NAMES: BUS Business, General; BUSN Any type of business
DESCRIPTORS: **Catheter** industry--Product development
PRODUCT/INDUSTRY NAMES: 3841544 (**Blood Vessel** Dilators)
SIC CODES: 3841 Surgical and medical instruments
FILE SEGMENT: NW File 649

InterVentional Technologies Announces Successful Completion of FullFlow Perfusion Dilation Catheter **Trials.**

TEXT:
...the successful completion of an extensive series of animal trials of the FullFlow perfusion dilation **catheter** .
... Washington, D.C. They conclusively demonstrate the device's capability to effectively and safely dilate **coronary arteries** while allowing near normal physiologic blood- **flow rates** throughout the procedure.
The FullFlow perfusion dilation **catheter** replaces the traditional **angioplasty balloon** with a retracting spring mesh. When deployed in the vessel, this mesh forms a scaffold...

...for blood flow, while at the same time providing significant radial dilating force. This new **catheter** facilitates prolonged vessel dilation without risk of **ischemia** or infarction.
Commenting on Segal's results, Rob Michiels, InterVentional Technologies' president and chief operating officer, noted: "Not only does this over-the-wire **catheter** allow more than three times the blood flow of currently marketed perfusion dilation **balloons** , it also permits side-branch perfusion and eliminates the need for a **balloon inflation** /deflation device.
"This is a significant breakthrough for high-risk patients receiving **angioplasty** treatment."
The company is assembling these data into an appropriate regulatory submission and plans to...
...San Diego; Murietta, Calif.; and Letterkenny, Ireland.
The company manufactures and markets worldwide, the TEC **thrombectomy catheter** , the Cutting **Balloon** microsurgical dilation **catheter** , the TRACKWIRE family of guide wires, the LP Stent, the INFILTRATOR **arterial** -wall **drug - delivery catheter** and the IRADIATOR **arterial** -wall radiotherapy system (see note). -0-
NOTE TO EDITORS: Some products are investigational use only...

DESCRIPTORS: **Catheter** industry...
PRODUCT/INDUSTRY NAMES: 3841544 (**Blood Vessel** Dilators)
19980305

39/5,K/22 (Item 15 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

06722964 SUPPLIER NUMBER: 14405696 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Prehospital-initiated vs hospital-initiated thrombolytic **therapy: the myocardial infarction triage and intervention trial.**
Weaver, W. Douglas; Cerqueira, Manuel; Hallstrom, Alfred P.; Litwin, Paul E.; Martin, Jenny S.; Kudenchuk, Peter J.; Eisenberg, Mickey
JAMA, The Journal of the American Medical Association, v270, n10, p1211(6) Sept 8, 1993
ISSN: 0098-7484 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT; ABSTRACT
WORD COUNT: 5603 LINE COUNT: 00470

ABSTRACT: Beginning **thrombolytic** therapy for heart attacks before hospital admission did not significantly improve patients' chances for survival or reduce complications. However, treatment begun within 70 minutes of the onset of symptoms reduced the number of complications and lessened the impact of the attack. **Thrombolytic** therapy is used to dissolve **blood clots** or prevent them from forming. A total of 360 patients who called paramedics and were suspected of having a heart attack were randomly assigned to one of two groups. One group received aspirin and **thrombolytic** therapy before arriving at the hospital; the other group did not. Patients who received treatment before arriving at the hospital began treatment 33 minutes earlier than the other patients. Measurements of the outcome of the two treatment strategies did not differ between the two groups.
AUTHOR ABSTRACT: Objective.--To determine the effect of prehospital-initiated vs hospital-initiated treatment of myocardial infarction on clinical outcome. Design.--Randomized, controlled clinical trial. Setting.--Multicenter study involving 19 hospitals and all paramedic systems in the Seattle, Wash, metropolitan area. Patients.--A total of 360 patients with symptoms for 6 hours or less, no risk factors for serious bleeding, and ST-segment elevation were selected by paramedics and a remote physician for inclusion into the trial. They represented 4% of patients with chest pain who were screened and 21% of those with acute infarction. Interventions.--Patients were allocated to have aspirin and alteplase treatment initiated before or after hospital arrival. **Intravenous** sodium heparin was administered to both groups in the hospital. Main Outcome Measure.--The primary endpoint was a ranked composite score (combining death, stroke, serious bleeding, and infarct size). The relation between time to treatment and outcome (composite score, infarct size, ejection fraction, and mortality) was also assessed. Results.--Initiating treatment before hospital arrival decreased the interval from symptom onset to treatment from 110 to 77 minutes (P<.001). Although more patients whose therapy was initiated before hospital arrival had resolution of pain by admission (23% vs 7%; P<.001), there were no significant differences in the composite score (P=.64), mortality (5.7% vs 8.1%), ejection fraction (53% vs 54%), or infarct size (6.1 % vs 6.5%). A secondary analysis of time to treatment and outcome showed that treatment initiated within 70 minutes of symptom onset was associated with better outcome (composite score, P=.009; mortality, 1.2% vs 8.7%, P=.04; infarct size, 4.9% vs 11.2%, P<.001; and ejection fraction, 53% vs 49%, P=.03) than later treatment. Identification of patients eligible for **thrombolysis** by paramedics reduced the hospital treatment time from 60 minutes (for patients not in the study) to 20 minutes (for study patients allocated to begin treatment in the hospital). Conclusion.--There was no improvement in outcome associated with initiating treatment before hospital arrival; however, treatment within 70 minutes of symptom onset--whether in the hospital or in the field--minimized the infarct process and its complications. (JAMA. 1993;270:1211-1216)

SPECIAL FEATURES: illustration; table; graph; chart
INDUSTRY CODES/NAMES: HLTH Healthcare
DESCRIPTORS: Heart attack--Care and treatment; **Thrombolytic** therapy--Administration and dosage; Triage (Medicine)--Evaluation
FILE SEGMENT: MI File 47

Prehospital-initiated vs hospital-initiated thrombolytic **therapy: the**

myocardial infarction triage and intervention trial.
ABSTRACT: Beginning **thrombolytic** therapy for heart attacks before hospital admission did not significantly improve patients' chances for survival...

...onset of symptoms reduced the number of complications and lessened the impact of the attack. **Thrombolytic** therapy is used to dissolve **blood clots** or prevent them from forming. A total of 360 patients who called paramedics and were...

...heart attack were randomly assigned to one of two groups. One group received aspirin and **thrombolytic** therapy before arriving at the hospital; the other group did not. Patients who received treatment...
...AUTHOR ABSTRACT: Patients were allocated to have aspirin and alteplase treatment initiated before or after hospital arrival. **Intravenous** sodium heparin was administered to both groups in the hospital. Main Outcome Measure.--The primary...

...ejection fraction, 53% vs 49%, P=.03) than later treatment. Identification of patients eligible for **thrombolysis** by paramedics reduced the hospital treatment time from 60 minutes (for patients not in the...

TEXT:
SEVERAL placebo-controlled trials of **intravenous thrombolytic** therapy have shown the greatest mortality reduction in the subset of patients with acute myocardial infarction receiving **thrombolytic** therapy in the first hour from symptom onset.[1-4]
... evaluation in the emergency department, and treatment after admission, it is virtually impossible to provide **thrombolytic** drug treatment within the first hour of symptoms to any meaningful proportion of patients with...

...physicians staff ambulances, it was shown in a nonrandomized comparison that very early initiation of **thrombolytic** drug treatment was associated with improved global left ventricular function.[5] Prehospital emergency care in...

...a variety of medical emergencies, primarily using protocol-driven approaches.
To evaluate whether prehospital-initiated **thrombolytic** drug treatment is feasible, safe, and beneficial for patients, a prospective, randomized, controlled trial of prehospital-initiated vs hospital-initiated **thrombolytic** therapy was performed.
METHODS
Patient Identification and Treatment The criteria used to select patients for prehospital initiation of **thrombolytic** therapy have been described.[6] All 15 prehospital care teams in the Seattle, Wash, metropolitan...

...those who consented (only one refused) were randomized to receive either prehospital- or hospital-initiated **thrombolytic** drug treatment. Full written information was provided and consent for follow-up was obtained from...

...pump) was available in the emergency department. All patients received standard basic medical care (oxygen, **intravenous cannulation** , and rhythm monitoring) during the prehospital treatment period. In addition, morphine sulfate was used for...

...patient groups at the time of hospital arrival. A 5000-U bolus, followed by continuous **intravenous** infusion, was administered for at least 48 hours. The **infusion rate** was adjusted by activated **thromboplastin** -time testing to maintain a 60- to 100-second range. The design and methods of...total of 360 patients were identified for randomization in the trial, 175 to prehospital-initiated **thrombolysis** , and 185 to hospital-initiated **thrombolysis** (Fig 1). Also, 130 patients with ST elevation were not enrolled in the trial. Most hospital arrival was 15 minutes longer for the

prehospital **thrombolysis** group, reflecting the time required to mix and initiate the **infusion** of alteplase. The total time from symptom onset to treatment for the prehospital- and hospital...

...33 [+ or -] 18 minutes. The cumulative distributions of time from symptom onset to initiation of **thrombolytic** therapy are depicted in Fig 2. Both groups were treated relatively soon after symptom onset...

...175 prehospital-allocated patients and all but 23 of the 185 hospital-allocated patients received **thrombolytic** therapy (overall, 336 of 360, or 93%). Of those not receiving **thrombolytic** drug treatment after randomization, some died before treatment could be initiated (n=4), had direct **coronary angioplasty** as an alternative treatment after initial physician assessment in the hospital (n=6), or were...

...also for those patients allocated to hospital-initiated treatment. A total of 579 patients received **thrombolytic** therapy in the same hospitals during the period of the trial, but were not randomized onset to receipt of **thrombolytic** therapy.

Three quarters of patients treated within 3 hours had an infarct size of 10...

...to determine, with a high degree of certainty, whether a patient was a candidate for **thrombolytic** therapy.

Computer-interpreted ECG was useful in enhancing selection accuracy and helped to minimize interpretation...

...elevation, its high specificity seems useful to nonexperts in excluding patients with nondiagnostic ECGs for **thrombolytic** treatment, and thus this approach should be considered in other situations in which expert consultation...

...carefully validated before being used for this purpose.[23]

No evidence suggested that paramedic-initiated **thrombolytic** therapy was associated with more complications. The incidence of cardiac arrest following treatment was low...

...and overlapped the reported rates for prior larger trials in which the combination of aspirin, **intravenous** heparin, and **thrombolytic drugs** have been **administered** .

When prehospital notification of the patient's condition was provided to the receiving hospital, as...
...to the hospital-treatment group were treated 40 minutes faster than concurrent, nonrandomized patients receiving **thrombolytic** therapy in the same hospitals. Except for the patients treated in this clinical trial, hospital...

...patients receiving prehospital-initiated and hospital-initiated treatment.

Unlike other reports evaluating the effects of **thrombolytic** therapy, essentially all patients received treatment within the first 3 hours of symptom onset. In...

...not be explained by other baseline variables. This positive effect of very early use of **thrombolytic** therapy further extends observations of others.[5,30]

Remarkably, 40% of all patients treated during...

...essentially aborted. This marked attenuation in infarct size is in contrast to previous western Washington **thrombolysis** trials, including a recent one in which alteplase was used in the emergency department but...

...had infarct sizes of 10% or less.[31]

The excellent outcomes associated with very early **administration** of **thrombolytic drugs** have several implications. The findings point out the need for public education programs aimed at...

...physicians and nurses are aware of the excessive in-hospital treatment

times for patients receiving **thrombolysis** , hospital delays in the United States, with very few exceptions, have remained relatively constant at...

...plan in most hospitals. In the Global Utilization of Streptokinase and Tissue Plasminogen Activator for **Occluded Coronary Arteries** (GUSTO) **thrombolysis** trial, the average delay before treatment in US hospitals was almost 80 minutes; only 3...30-minute standard for treatment can be achieved for the vast majority of patients receiving **thrombolytic** therapy.

In summary, this randomized trial evaluating the strategy of prehospital initiation of **thrombolytic** drug therapy by paramedics showed that appropriate patient selection is possible using the screening skills ...

...demonstrates that through protocol-driven approaches that include prehospital identification of potentially eligible patients for **thrombolysis** , hospital treatment times can be substantially reduced from the current 60 to 90 minutes to...

...References

[1.] Gruppo Italiano per lo Studio della Streptochinase nell' Infarto miocardio (GISSI). Effectiveness of **intravenous thrombolytic** treatment in acute myocardial infarction. Lancet. 1986;1:397-402. [2.] ISIS-2 (Second International Study of Infarct Survival Collaborative Group). Randomized trial of **intravenous** streptokinase, oral aspirin, both or neither among 17 187 cases of suspected acute myocardial infarction...

...tissue plasminogen activator for mortality reduction in acute myocardial infarction: Anglo-Scandinavian Study of Early **Thrombolysis** (ASSET). Lancet. 1988;2:525-530. [4.] AIMS Trial Study Group. Effect of **intravenous** APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial...

...Koren G, Weiss AT, Hasin Y, et al. Prevention of myocardial damage in acute myocardial **ischemia** by early treatment with **intravenous** streptokinase. N Engl J Med. 1985;313:1384-1389. [6.] Weaver WD, Eisenberg ME, Martin...

...Infarction Triage and Intervention Project--phase I: patient characteristics and feasibility of prehospital initiation of **thrombolytic** therapy. J Am Coll Cardiol. 1990;15:925-931. [7.] Kudenchuk PJ, Ho MT, Weaver WD, et al. Accuracy of computer-interpreted electrocardiography in selecting patients for **thrombolytic** therapy. J Am Coll Cardiol. 1991;17:1486-1491. [8.] Weaver WD, Kennedy JW. Myocardial infarction-**thrombolytic** therapy in the prehospital setting. In: Fuster V, Verstraete M, eds. **Thrombosis** in Cardiovascular Disorders. Philadelphia, Pa: Harcourt Brace & Co; 1992:275-287. [9.] Ritchie JL, Davis KB, Williams DL, et al. Global and regional left ventricular function and tomographic **radionuclide perfusion** : the Western Washington Intracoronary Streptokinase in Acute Myocardial Infarction Trial. Circulation. 1984;70:867-875...

...GE, et al. Milwaukee Prehospital Chest Pain Project--phase I: feasibility and accuracy of prehospital **thrombolytic** candidate selection. Am J Cardiol. 1992;69:991-996. [13.] Gibler WB, Kereiakes DJ, Dean...

...J. 1991;121:1-11. [14.] Schofer J, Buttner J, Geng G, et al. Prehospital **thrombolysis** in acute myocardial infarction. Am J Cardiol. 1990;66:1429-1433. [15.] Varshavsky SY. Prehospital **thrombolysis** in acute myocardial infarction. Prehospital Disaster Med. 1992;7:57-59. [16.] **Thrombolysis** Early in Acute Heart Attack Trial Study Group. Very early **thrombolytic** therapy in suspected acute myocardial infarction. Am J Cardiol. 1990;65:401-407. [17.] Villemant D, Barriot P, Riou B, et al. Achievement of **thrombolysis** at home in cases of acute myocardial infarction. Lancet. 1987;1:228-229. [18.] Barbash...

...Roth A, Hod H, et al. Randomized controlled trial of late in-hospital angiography and **angioplasty** versus conservative management after treatment with recombinant tissue-type plasminogen activator in acute

myocardial infarction...

...Cardiol. 1990;66:538-545. [19.] Weiss AT, Fine DG, Applebaum D, et al. Prehospital **coronary thrombolysis** : a new strategy in acute myocardial infarction. Chest. 1987;92:124-128. [20.] Bossaert LL, Demey HE, Colemont LJ, et al. Prehospital **thrombolytic** treatment of acute myocardial infarction with anisoylated plasminogen streptokinase activator complex. Crit Care Med. 1988...Med. 1991:325:1767-1773. [24.] Roth A, Barbash GI, Hod H, et al. Should **thrombolytic** therapy be **administered** in the mobile intensive care unit in patients with evolving myocardial infarction? J Am Coll...

...Schmidt SB, Borsch MA. The prehospital phase of acute myocardial infarction in the era of **thrombolysis** . Am J Cardiol. 1990;65:1411-1415. [26.] Brugeman J, van der Meer J, de Graeff PA, Takens LH, Lie KI. Logistical problems in prehospital **thrombolysis** . Eur Heart J. 1992;13:787-788. [27.] Mayo E. The Human Problems of an...

...28.] Sharkey SW, Brunette DD, Ruiz E, et al. An analysis of time delays preceding **thrombolysis** for acute myocardial infarction. JAMA. 1989;262:3171-3174. [29.] Kereiakes DJ, Weaver WD, Anderson...

...780. [30.] Fine DG, Weiss AT, Sapoznikov D, et al. Importance of early initiation of **intravenous** streptokinase therapy for acute myocardial infarction. Am J Cardiol. 1986;58:411-417 [31.] Cerqueira...

...Ritchie JL. Radionuclide assessment of infarct size and left ventricular function in clinical trials of **thrombolysis** . Circulation. 1991;84(suppl I):100-108. [32.] Pell CH, Miler HC, Robertson CE, Fox...

...DESCRIPTORS: **Thrombolytic** therapy
19930908

39/5,K/28 (Item 21 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

06156208 SUPPLIER NUMBER: 12721944 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Reperfusion and revascularization strategies for coronary artery **disease in women.**
Eysmann, Susan B.; Douglas, Pamela S.
JAMA, The Journal of the American Medical Association, v268, n14, p1903(5)
Oct 14, 1992
ISSN: 0098-7484 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT; ABSTRACT
WORD COUNT: 5363 LINE COUNT: 00444

ABSTRACT: A review of the literature on the treatment of **coronary artery** disease found that women may benefit from many of the strategies used on men, including **thrombolytic** drugs, percutaneous transluminal **coronary angioplasty** (PTCA) and **coronary artery** bypass grafting (CABG). **Thrombolytic** drugs break up the **blood clots** that cause most heart attacks. **Thrombolytic** therapy substantially reduces mortality after a heart attack in both men and women, although the reduction in mortality is not as great in women as it is in men. PTCA was initially found to be less effective in women, but this may have been because the **balloons** used were too big. The studies show that women have more complications during the procedure, but have a similar long-term outcome as men. The same is true for CABG; long-term survival is the same in women as in men, although fewer women may experience relief from angina. The higher complication rate in women may be a reflection of their older age.
AUTHOR ABSTRACT: Objective.--One third of all deaths in women in the United States each year are attributable to **coronary** heart disease. Gender differences exist in the course and management of patients with **coronary** heart disease. Few randomized trials have been conducted in women to evaluate effective therapeutic strategies. With the aim of developing rational approaches to women with **coronary** heart disease, we review gender-related outcomes with **coronary** revascularization and reperfusion

therapies.

Data Source.--English-language journal articles and reviews on the subject of women with **coronary** heart disease or gender-specific responses to **coronary** heart disease management, from 1970 through 1992, identified through MEDLINE searching.

Study Selection. Selected studies included only randomized controlled trials for topics related to **thrombolysis** , and articles considered to contribute significantly to the topic of women with **coronary artery** disease in the case of **angioplasty** and **coronary artery** bypass grafting.

Data Extraction.--Two reviewers participated in extracting the data with the aim of presenting a balanced and comprehensive review of the subject.

Data Synthesis.-- **Thrombolysis** in acute myocardial infarction reduces mortality in men and women, although women may have a reduced mortality benefit compared with men. **Angioplasty** and the newer interventional devices result in greater procedural morbidity but similar if not better long-term outcomes in women. Women may have a greater mortality rate than men with **coronary artery** bypass surgery, although studies suggest that outcome after bypass surgery may depend more on **coronary** size and preoperative risk factors than on gender itself.

Conclusions. The existence of gender differences in the course of **coronary** heart disease and response to revascularization and reperfusion strategies suggests the need for unique clinical approaches to the female patient with **coronary** heart disease and stresses the importance of developing randomized trials that enroll adequate numbers of women and that are designed to answer genderspecific questions.

SPECIAL FEATURES: illustration; table
INDUSTRY CODES/NAMES: HLTH Healthcare
DESCRIPTORS: **Coronary** heart disease--Care and treatment; **Thrombolytic** therapy--Demographic aspects; **Coronary artery** bypass--Demographic aspects; Transluminal **angioplasty** --Demographic aspects; Women--Diseases
FILE SEGMENT: MI File 47

Reperfusion and revascularization strategies for coronary artery **disease in women.**

ABSTRACT: A review of the literature on the treatment of **coronary artery** disease found that women may benefit from many of the strategies used on men, including **thrombolytic** drugs, percutaneous transluminal **coronary angioplasty** (PTCA) and **coronary artery** bypass grafting (CABG). **Thrombolytic** drugs break up the **blood clots** that cause most heart attacks. **Thrombolytic** therapy substantially reduces mortality after a heart attack in both men and women, although the...

...initially found to be less effective in women, but this may have been because the **balloons** used were too big. The studies show that women have more complications during the procedure...
...AUTHOR ABSTRACT: third of all deaths in women in the United States each year are attributable to **coronary** heart disease. Gender differences exist in the course and management of patients with **coronary** heart disease. Few randomized trials have been conducted in women to evaluate effective therapeutic strategies. With the aim of developing rational approaches to women with **coronary** heart disease, we review gender-related outcomes with **coronary** revascularization and reperfusion therapies.

Data Source.--English-language journal articles and reviews on the subject of women with **coronary** heart disease or gender-specific responses to **coronary** heart disease management, from 1970 through 1992, identified through MEDLINE searching.

Study Selection. Selected studies included only randomized controlled trials for topics related to **thrombolysis** , and articles considered to contribute significantly to the topic of women with **coronary artery** disease in the case of **angioplasty** and **coronary artery** bypass grafting.

Data Extraction.--Two reviewers participated in extracting the data with the aim of presenting a balanced and comprehensive review of the subject.

Data Synthesis.-- **Thrombolysis** in acute myocardial infarction

reduces mortality in men and women, although women may have a reduced mortality benefit compared with men. **Angioplasty** and the newer interventional devices result in greater procedural morbidity but similar if not better long-term outcomes in women. Women may have a greater mortality rate than men with **coronary artery** bypass surgery, although studies suggest that outcome after bypass surgery may depend more on **coronary** size and preoperative risk factors than on gender itself.

Conclusions. The existence of gender differences in the course of **coronary** heart disease and response to revascularization and reperfusion strategies suggests the need for unique clinical approaches to the female patient with **coronary** heart disease and stresses the importance of developing randomized trials that enroll adequate numbers of...

TEXT:

...disease is the leading cause of death in men and women in the United States. **Coronary** heart disease accounts for 250000 deaths in US women each year and is responsible for...

...in US women. Nevertheless, a number of recent studies suggest that physicians' diagnostic approaches to **coronary** heart disease and subsequent treatment strategies may be less aggressive in women than in men ...

...poor accuracy of stress testing in women, to the perception of a low prevalence of **coronary** disease and of a good outcome from **coronary** disease in women, and to differences in medical care offered to men and women. Since gender differences in the underlying pathophysiology of **coronary** disease and in the response to therapeutic interventions may justify differential treatment, the significance of...

Reperfusion and revascularization utilizing **thrombolysis** , **angioplasty** , and bypass surgery are the mainstays of significant **coronary** heart disease management. However, few randomized trials have been conducted in women to evaluate strategies based on these techniques. We will review the data on the effectiveness of **thrombolysis** in acute myocardial infarction and of revascularization using percutaneous transluminal **coronary angioplasty** (PTCA) and **coronary artery** bypass grafting (CABG) in women. The available data do not directly compare the risks and...

...decision making. They do, however, establish the existence of gender differences in the course of **coronary** heart disease and in the response to revascularization strategies, underscoring the need for unique clinical approaches to the female patient.

THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION

Studies vary as to whether the immediate and long-term prognosis...

...most available studies of gender-related prognosis after myocardial infarction predate the widespread use of **thrombolysis** in the management of acute myocardial infarction, so that few data are available for mortality...

...studies have revealed no significant differences in the pharmacokinetics of tissue-type plasminogen activator or **coronary artery** patency rates in men vs women in the setting of acute myocardial infarction.[14] Most important, **intravenous thrombolytic** therapy in acute myocardial infarction reduces mortality rates in both sexes. Nevertheless, gender differences in mortality rates have been found in subgroup analyses. The Table reviews the major **thrombolysis** trials that have reported mortality data by gender. The second International Study of Infarct Survival (ISIS2) [15] is the largest published trial of **thrombolysis** in acute myocardial infarction. This study randomized 3945 women and 13 125 men to **intravenous** streptokinase therapy, oral aspirin therapy, both, or neither. Both men and women benefited most from...

...della Streptochinasi nell'Infarto Miocardico, part 1 (GISSI-1), [16,17] and several other, smaller **thrombolysis** trials (Anglo-Scandinavian Study of Early **Thrombolysis** [ASSET],[18] European Working Party,[19] and Western Washington Trial [20,21]) in the Table, three patterns become apparent. First, **intravenous thrombolysis** therapy clearly reduced

mortality rates in the setting of an acute myocardial infarction in both...

...after myocardial infarction were higher among women than among men in both the placebo and **thrombolysis** groups. Third, GISSI excluded, these randomized trials have shown a relatively lower reduction in mortality...

...of women presenting with myocardial infarction contributes to their relatively lesser reduction in mortality after **thrombolysis** . However, data from GISSI-2, a randomized trial comparing streptokinase therapy alone, streptokinase therapy plus...

...less effective preservation of myocardial function, or that women have more frequent cardiac events after **thrombolysis** . Unfortunately, genderspecific differences in recovery of left ventricular function or recurrent cardiac events have not...

...be more prevalent in women, especially younger women; while clearly speculative, if this were true, **thrombolysis** might be less effective among women than among men, in whom **coronary thrombosis** is thought to be nearly universal.

Another hypothesis is that women have a greater number of complications with **thrombolysis** than men, in part because they are older. In the **Thrombolysis** and **Angioplasty** in Myocardial Infarction (TAMI) trials, female gender was not an independent predictor of inhospital mortality...

...elderly women compared with all other patients enrolled, independent of infarct vessel patency and subsequent **angioplasty** success rate. [23] In the **Thrombolysis** in Myocardial Infarction (TIMI) phase II trial, patients received a 100-mg dose of recombinant tissue-type plasminogen activator and were randomized to a conservative strategy in which **coronary** angiography was performed only if there was recurrent spontaneous or exercise-induced **ischemia** . With this treatment, 5.9% of women v s 3.8% of men had a...

...and emphasize the potential importance of weight-, age-, and/or gender-based dosage modification of **thrombolytic** agents, issues that have not been adequately addressed by many **thrombolysis** trials to date. Recent data from the GISSI-2 study also demonstrated an excess of...a circumstance unique to women, there are no published data regarding the bleeding risks of **thrombolysis** therapy in the rare menstruating woman who presents with myocardial infarction.

Finally, although the Table reveals lower relative reductions in mortality rates with **thrombolysis** in women than in men, absolute reductions appear similar. For example, in ISIS-2, **thrombolysis** reduced the mortality rate from 17.5% to 12.2% in women, a 5.3...

...function of their high underlying mortality rates with myocardial infarction and less a failure of **thrombolysis** . This observation suggests that there are other factors, which **thrombolysis** cannot change, that may complicate the course of myocardial infarction in women, leading to high mortality rates. Factors that may be important include patient age, infarct size, reperfusion rates, **coronary flow rates** , persistent **ischemia** , concurrent illnesses, or ventricular remodeling. At present, these issues can only be addressed by multivariable...

...emphasizes the need for further research in this subset of patients. Since most trials of **thrombolytic** therapy have had an upper age limit of 70 or 75 years, fewer women than men have been enrolled in trials, and the value of **thrombolysis** in the very elderly remains somewhat controversial. Whether older age alone explains the relative underenrollment of women in **thrombolysis** trials is largely unexplored. One study has suggested that only 55% of eligible women compared...

...and men who were not treated. [26] These data coupled with the known efficacy of **thrombolysis** in both sexes suggest that gender bias may be playing a role in the selection of patients for **thrombolysis** . If so, the reduced mortality benefit in women is of particular concern, since one might...

...women were treated compared with higher-risk men.

At present, in women as in men, **thrombolysis** offers the greatest potential pharmacologic reduction in mortality during acute myocardial infarction and should not...

...research should be directed at examining current databases for gender-related differences in response to **thrombolysis** and ensuring the enrollment of adequate numbers of women (and elderly) in **thrombolysis** trials. A better understanding of why women have shown a reduced mortality benefit compared with...

...rate (1.8% vs 0.7%). Women had a higher incidence of intimal tears and **coronary** dissections than men. Female gender was an independent correlate of reduced success with **angioplasty** . [27] Two other studies examined gender differences in acute outcomes following **angioplasty** during the technique's early development, from 1980 to 1986 [28] and from 1979 to...

...1985.[29]

It has been suggested that the early use of 3.0-mm PTCA **balloons** , which were often oversized for women, predisposed them to complications with subsequent increased in-hospital...

...While acute clinical and angiographic success rates appear worse in women, long-term outcome and **restenosis** rates appeared at first to be better in women than in men. In the initial National Heart, Lung, and Blood Institute series (1982), after successful **angioplasty** , women had similar symptomatic improvement, higher event-free survival (80% vs 69%), and lower cumulative...

...months after PTCA but more frequent anginal symptoms in women. Numerous studies have reported lower **restenosis** rates in women than in men,[30-33] but this finding is far from universal...

...from the Cleveland Clinic [34,35] failed to identify gender as a risk factor for **restenosis** after PTCA. Furthermore, in a careful meta-analysis that reviewed 212 published reports on **angioplasty** and selected the 31 reports most likely to have reported unbiased results, gender was not found to be significantly correlated with post-PTCA **restenosis** .[36] Since most studies of **restenosis** are limited by incomplete angiographic follow-up, varying definitions of **restenosis** , and lack of multivariable analysis, the role of gender in the mechanism and rate of **restenosis** is uncertain but likely to be small.

Recently, the Cleveland Clinic has published preliminary data showing that, among patients who underwent **coronary** atherectomy, women had a higher complication rate than men. [37] By multivariable analysis, female gender...

...major complication rates (emergency surgery, death, or myocardial infarction) but more frequent minor complications (transfusion, **vascular** surgery, or non-Q-wave myocardial infarction) than men.[38] In recent reports of predictors of **restenosis** following intracoronary stenting and directional atherectomy, [39,40] gender was again not found to be...

...suggest that PTCA and the newer interventional devices carry higher procedural morbidity in women with **coronary** disease, few studies have adjusted these data for the baseline discrepancies in age, **coronary** size, and concurrent illness between men and women. Favorable long-term outcome suggests that percutaneous...

...option in women. The precise reason for women's increased morbidity at the time of **angioplasty** requires further study.

CORONARY ARTERY BYPASS GRAFTING

Several studies have examined by gender the preoperative characteristics, operative mortality rates, symptom relief, and long-term survival of patients undergoing **coronary artery** bypass surgery. The majority of studies have examined operative results from the 1970s and early 1980s and do not include more recent advances, such as internal mammary **artery** grafting, advances in cardioplegia, routine antiplatelet

therapy, and aggressive lipid-lowering therapy after surgery. Both...

...gender comparisons of the morbidity and mortality of CABG is unknown.

As in the early **angioplasty** studies, women who have undergone **coronary artery** bypass surgery have been older and have had more severe anginal symptoms and more unstable...

...women. In one study, when matched for preoperative angina severity and the number of diseased **blood vessels** , women and men had equal mortality rates. [46] In another study, when the authors adjusted...

...body surface area, gender was no longer an important risk factor for operative death. [44] **Coronary Artery** Surgery Study (CASS) investigators have found that mortality differences for men and women were primarily a result of differences in **coronary artery** size. [56] However, such corrections do not fully account for gender differences in outcome in...

...gender-related differences in referrals for CABG/PTCA in patients who had already had cardiac **catheterization** . [58,59] Thus, if gender bias exists, it is more likely in the referral of...
...62]

These studies suggest that outcome after CABG may depend more on patient size or **coronary** size and preoperative risk factors than on gender itself. Although women have a higher surgical...

...to CABG, their long-term survival is similar to that of men. With internal mammary **artery** grafting, more aggressive lipid-lowering and antiplatelet therapy, and aggressive use of a variety of...

...described will need to be reevaluated.

COMMENT

A critical issue in caring for women with **coronary artery** disease is knowledge of not just the operative risk of bypass surgery in women vs men but the medical risk for women. The **Coronary Artery** Surgery Study has yet to publish the results of medical vs surgical therapy in its...that take into account the existence of gender differences in the presentation and course of **coronary artery** disease are more likely to provide clinically valuable information.

Revascularization, whether medically through **thrombolysis** ; mechanically through **angioplasty** , atherectomy, or intracoronary stents; or surgically, is an immensely important component of the treatment of **coronary artery** disease. As this review has suggested, gender differences exist in the course and treatment of patients with **coronary artery** disease. Compared with men, women receive less benefit from **thrombolysis** in myocardial infarction, suffer more acute complications from **coronary** interventions, and may have a greater early mortality rate with bypass surgery. Rational therapy at the present time would consist of aggressive **administration** of **thrombolysis** to women with acute myocardial infarction. Future studies should continue to address the issue of...

...dosages in the petite woman and/or the elderly woman who might thereby benefit from **thrombolysis** without increased complications as well as investigation of other factors that may predispose to hemorrhagic...

...and CABG are offered to women, such decisions should be individualized, based on the patients' **coronary** anatomy and preoperative risk factors, as in men, but also with full consideration of morbidity...

...revascularization with medical treatment in women alone.

There are many gaps in our knowledge of **coronary** heart disease in women. The existence of gender differences suggests the need for unique clinical...

...References

1. Tobin JN, Wassertheil-Smoller S, Wexler JP, et al. Sex bias in considering **coronary** bypass surgery. Ann Intern Med. 1987;107:19-25.

2. Steingart RM, Packer M, Harem P, et al. Sex differences in the

management of **coronary artery** disease. N Engl J Med. 1991;325:226-230.
3. Khan SS, Nessim S, Gray R, et al. Increased mortality of women in **coronary artery** bypass surgery: evidence for referral bias. Ann Intern Med. 1990;112:561-567.
4. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for **coronary** heart disease. N Engl J Med. 1991;325:221-225.
5. Maynard C, Litwin PE...

...and men in survival after myocardial infarction. JAMA. 1990;263:1092-1096.
14. Becket RC. **Coronary thrombolysis** in women. Cardiovasc Dis Women. 1990;77(suppl 2):110-123.
15. ISIS-2 Collaborative Group. Randomized trial of **intravenous** streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction...

...360.
16. Gruppo Italiano per 10 Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Effectiveness of **intravenous thrombolytic** treatment in acute myocardial infarction. Lancet. 1986;1:397-402.
17. Gruppo Italiano per 10 Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Long-term effects of **intravenous thrombolysis** in acute myocardial infarction: final report of the GISSI study. Lancet. 1987;2:871-874.
18. Anglo-Scandinavian Study of Early **Thrombolysis** (ASSET). Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. Lancet. 1988...

...3:325-331.
20. Kennedy JW, Martin GV, Davis KB, et al. The Western Washington **intravenous** streptokinase in acute myocardial infarction randomized trial. Circulation. 1988;77:345-352.
21. Kennedy JW...

...3236.
23. Topol E J, Califf RM, George BS, et al. Insights derived from the **Thrombolysis** and **Angioplasty** in Myocardial Infarction (TAMI) trials. J Am Coll Cardiol. 1988;12:24A-31A.
24. Bovill...
...Santoro E, et al. The risk of stroke in patients with acute myocardial infarction after **thrombolytic** and antithrombotic treatment. N Engl J Med. 1992;327:1-6.
26. Maynard C, Althouse R, Cerqueira M, et al. Underutilization of **thrombolytic** therapy in eligible women with acute myocardial infarction. Am J Cardiol. 1991;68:529- ...Mullin SM, Kelsey SF, et al. Sex differences in early and long-term results of **coronary angioplasty** in the NHLBI PTCA registry. Circulation. 1985;71:90-97.
28. McEniery PT, Hollman J, Knezınek V, et al. Comparative safety and efficacy of percutaneous transluminal **coronary angioplasty** in men and in women. Cathet Cardiovasc Diagn. 1987;13:364-371.
29. Cowley MJ, Kelsey SF, Costigan TM, et al. Percutaneous transluminal **coronary angioplasty** in women: gender differences in outcome. In: Eaker ED, Packard B, Wenget NK, Clarkson T, Tyroler HA, eds. **Coronary Artery** Disease in Women. New York, NY: Haymarket-Doyma; 1987:251-256.
30. Holmes DR Jr, Holubkov R, Vliestra RE, et al. Comparison of complications during percutaneous transluminal **coronary angioplasty** from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. J Am Coll Cardiol. 1998;12:1149-1155.
31. Ellis SG. Elective **coronary angioplasty** : techniques and complications. In: Topol E J, ed. Textbook of Interventional Cardiology. Philadelphia, Pa: WB Saunders Co; 1990:199-222.
32. Califf RM, Ohman M, Frid DJ, et al. **Restenosis** : the clinical issues. In: Topol EJ, ed. Textbook of Interventional Cardiology. Philadelphia, Pa: WB Saunders Co; 1990:363-394.
33. Califf RM, Fortin DF, Frid DJ, et al. **Restenosis** after

coronary angioplasty : an overview. J Am Coll Cardiol. 1991;17:2B-13B.
34. Hollman B, Badhwar K, Beck GJ, et al. Risk factors for recurrent **stenosis** following successful **coronary angioplasty** . Cleve Clin J Med. 1989;56: 517-523.
35. Arora RR, Konrad K, Badhwar K, et al. Resrenosis after transluminal **coronary angioplasty** : a risk factor analysis. Gather Cardiovasc Diagn. 1990; 19:17-22.
36. Bobbio M, Detrano R, Colombo A, et al. **Restenosis** rate after percutaneous transluminal **coronary angioplasty** : a literature overview. J Invas Cardiol. 1991;3:214-224.
37. Casale PN, Whitlow PL...

...Fishman RF, Friedrich SP, Gordon PC, et al. Acute and long-term results of new **coronary** interventions in women and the elderly. Circulation. In press.
39. Carrozza JP Jr, Kuntz RE...
...40. Fishman RF, Kuntz RE, Carrozza JP Jr, et al. Long-term results of directional **coronary** atheroctomy: predictore of **restenosis** . J Am Coll Cardiol. In press.
41. Loop FD, Lytle BW, Cosgrove DM, et al: Influence of the internal-mammary- **artery** graft on 19-year survival and other cardiac events. N Engl J Med. 1986;314:1-6.
42. Loop FD, Irarrazaval MJ, Breede JJ, et al. Internal mammary **artery** graft for **ischemic** heart disease. Am J Cardiol. 1977;39:516-522.
43. Chesebro JH, Clements IP, Fuster V, et al. A platelet-inhibitor-drug trial in **coronary - artery** bypass operations: benefit of perioperative dipyridamole and aspirin therapy on early postoperative **vein** -graft patency. N Engl J Med. 1982;307: 73-78.
44. Loop FS, Gelding LR, MacMillan JP, et al. **Coronary artery** surgery in women compared with men: analysis of risks and long-term results. JAm Coil...

...25:449-453.
46. Douglas JS, King SB, Jones EL, et al. Reduced efficacy of **coronary** bypass surgery in women. Circulation. 1981;64(suppl 2):11-16.
47. Eaker ED, Kronmal...

...et al. Comparison of the long-term, postsurgical survival of women and men in the **Coronary Artery** Surgery Study (CASS). Am Heart J. 1989;117:71-81.
48. Bolooki H, Vargas A, Green R, et al. Results of direct **coronary artery** surgery in women. J Thorac Cardiovasc Surg. 1975;69:271-277.
49. Khan SS. Why...

...Cardiol Board Rev. 1991;8:54-67.
50. Richardson JV, Cyrus RJ. Reduced efficacy of **coronary artery** bypass grafting in women. Ann Thorac Surg. 1986;42:S16-S21.
51. Kennedy JW, Kaiser...

...analysis of the clinical and angiographic predictors of operative mortality from the collaborative study in **coronary artery** surgery (CASS). J Thorac Cardiovasc Surg. 1980;80:876887.
52. Killen DA, Reed WA, Arnold M, et al. **Coronary artery** bypass in women: long-term survival. Ann Thorac Surg. 1982;34:559-563.
53. Hall RJ, Elayda MA, Gray A, et al. **Coronary artery** bypass: long-term follow-up of 22,284 consecutive patients. Circulation. 1983;68(suppl II...

...Heart J. 1984;5: 35-42.
55. Gardner TJ, Horneffer PJ, Gott VL, et al. **Coronary artery** bypass grafting in women. Ann Surg. 1985;2.01:780-784.
56. Davis KB. **Coronary artery** bypass graft surgery in women. In: Eaker ED, Packard B, Wenger NK, et al, eds. **Coronary Artery** Disease in Women. New York, NY: Haymarket-Doyma; 1987:247-250.
57. Fisher LD, Kennedy JW, Davis KB, et al. Association of sex, physical size, and operative mortality after **coronary artery** surgery (CASS). J Thorac Cardiovasc Surg. 1982;84:334-341.
58. Krumholz H, Douglas PS, Lauer MS, et al. Selection of patients

for **coronary** angiography and **coronary** revascularization early after myocardial infarction: is there evidence for a gender difference in the use ...

...116:785-790.

59. Bickell NA, Pieper KS, Lee KL, et al. Referral pattens for **coronary artery** disease treatment: gender basis or good clinical judgment? Ann Intern Med. 1992;116:791-797.

60. Johnson WD, Kayser KL, Pedraza PM. Angina pectoris and **coronary** bypass surgery: patterns of prevalence and recurrences in 3,105 consecutive patients followed up to 1197.

61. Golding LR, Groves LK. Results of **coronary artery** surgery in women. Cleve Clin Q. 1976;43: 113-115.

62. Myers WO, Davis K, Foster ED, et al. Surgical survival in the **Coronary Artery** Surgery Study (CASS) Registry. Ann Thorac Surg. 1985;40:245260.

This article is one of...

DESCRIPTORS: **Coronary** heart disease...

... **Thrombolytic** therapy...

... **Coronary artery** bypass...

...Transluminal **angioplasty** --
19921014

39/5,K/33 (Item 26 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

04619013 SUPPLIER NUMBER: 08810915 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Thrombolysis : **choosing an agent following myocardial infarction.**
Kleiman, Neal S.; Pratt, Craig M.; Roberts, Robert
Consultant, v30, n2, p29(6)
Feb, 1990
ISSN: 0010-7069 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT
WORD COUNT: 3792 LINE COUNT: 00320

SPECIAL FEATURES: illustration; photograph
INDUSTRY CODES/NAMES: HLTH Healthcare
DESCRIPTORS: Infarction--Drug therapy; Heart attack--Drug therapy; **Thrombolytic** drugs--Evaluation
SIC CODES: 8011 Offices & clinics of medical doctors
FILE SEGMENT: TI File 148

Thrombolysis : **choosing an agent following myocardial infarction.**

TEXT:
Choosing an Agent Following Myocardial Infarction The most important decisions involved in **administering** a **thrombolytic** agent are whether to use one at all and, if so, how to use it...
...infarction. (In part 2 of this series [page 39], we discuss selection of patients for **thrombolytic** therapy.) Of lesser importance is the question of which **drug** to choose. To date, the Food and **Drug Administration** has approved three **intravenous drugs** for treatment of myocardial infarction: streptokinase (in May 1987); tissue plasminogen activator (TPA, in December...
... 1985, compared the efficacy of TPA and streptokinase in establishing reperfusion and patency of totally **occluded** infarct vessels. In the National Heart, Lung, and Blood Institute **Thrombolysis** in Myocardial Infarction Phase I trial (TIMI I), [1] patients treated within 7 hours of...

...million U over 1 hour, or TPA IV, 80 mg over 3 hours.
Patients underwent **coronary arteriography** before receiving the assigned drug and again following documentation of total **occlusion** . After

they received the drug, serial **coronary arteriograms** were taken for 90 minutes. At the end of that time, reperfusion (defined as restoration of antegrade **coronary arterial** flow in a totally **occluded** vessel) had occurred in 62% of patients receiving TPA and 31% of those receiving streptokinase...

...in the second study, the European Cooperative Study Group trial, [2] were similar. No pretreatment **arteriograms** were performed in this study, so patients with spontaneous reperfusion were included among those with open vessels. Patency rates (the percentage of **coronary arteries** that were not **occluded** at the time the **arteriogram** was taken) were 55% and 70% for those treated with streptokinase and TPA, respectively, and...
...equal frequency in both treatment groups in both studies. Most of the bleeding occurred at **catheterization** access sites.

More recently, data have become available concerning the use of **intravenous** APSAC. In one study, [4] reperfusion rates following administration of APSAC were compared with those...

...to 6 hours of onset.

In a study comparing IV APSAC with IV streptokinase, [5] **arterial** patency was present 90 minutes after initiation of treatment in 55% of patients receiving APSAC...

...dosage, you can expect a 70% patency rate 90 minutes after initiating treatment. Digital subtraction **arteriography** (Figure) reveals appearance of a **coronary** vessel that was completely blocked by a **thrombus** (A) before treatment and (B) after circulation was restored following administration of TPA.

For patients...

...but heparin (bolus followed by infusion) should be started within the first few hours after **administration** of these **drugs** .

Although revised TPA dosing schedules are under investigation, higher dosages of suspension culture TPA are...
...heparin and aspirin. Moreover, with inclusion of those patients who did not undergo a predischarge **coronary arteriogram** because of death or a nonfatal reinfarction, the percentage of reocclusion in patients in both... 4% of patients receiving streptokinase and in 2% of those receiving conventional therapy. In the **Thrombolysis** and **Angioplasty** in Myocardial Infarction (TAMI) trial, [13] recurrent **ischemia** occurred in 18% of patients receiving **intravenous** TPA (without **angioplasty**); actual reocclusion of the infarct vessel occurred in fewer than half of these patients. In...

...OF DRUGS ON
MORTALITY

So far, four trials large enough to study the effect of **thrombolysis** on mortality have been completed; two used streptokinase, [12,16] one used TPA, [17] and...

...this mortality figure, you can see the difficulty inherent in showing a difference between two **thrombolytic** drugs. If streptokinase were to lead to a 25% reduction in hospital mortality, comparison of...

...group that would have a mortality of only 7.4%. If TPA, the more potent **thrombolytic** drug, were to lead to a 25% greater reduction in mortality, such a study would...

...occurred with equal frequency in both groups, early reperfusion could not be assessed directly because **coronary** angiography was not performed until an average of 4 days after treatment. At that time...

...present with a large, life-threatening infarction that prompts the decision for treatment with a **thrombolytic drug** . Because of its clearance mechanism, TPA should be **administered** with extreme caution to patients having liver disease.

Potential for Anaphylaxis. Since streptokinase is a...

...to it. Severe allergic reactions are extremely rare, but anaphylaxis has been reported. Do not **administer** this **drug** (or its derivative, APSAC) to patients who have received it within the past 6 months or who have had a recent streptococcal infection.

Additional aspects. When choosing a **thrombolytic** drug, keep in mind several practical considerations. Since (to the best of our knowledge) the proximate cause of acute myocardial infarction is **occlusive** intracoronary **thrombus** , TPA would ...Obviously, if only one of the drugs is available, it should be used without question.

THROMBOLYTIC AGENTS OF THE FUTURE

Several other **thrombolytic** drugs are expected to become available within the next few years.

Urokinase. Urokinase is another...

...14] This was particularly true in those cases where reperfusion failed and emergency of "salvage" **angioplasty** was performed; a significantly lower incidence of reocclusion followed. The authors speculated that the cause...

...another nonfibrin-specific agent may prove useful in patients with large infarctions for whom emergency **catheterization** and **angioplasty** are contemplated. Additional trials are under way, treating acute myocardial infarction with IV urokinase, but...

...with TPA. A combination of these two agents in very low doses has produced high **perfusion rates** in the small number of patients treated thus far, with remarkably little depletion of systemic...

...by intrinsic inhibitors of fibrinolysis. In addition, construction of "targeted" hybrid molecules containing both a **thrombolytic** drug and an antibody to fibrin is being studied as one means of increasing the...
...specific sites in the coagulation cascade, the use of which may complement the action of **thrombolytic** drugs. These agents includ specific inhibitors of **thrombin** , powerful platelet-inhibiting agents (**thromboxane** and serotonin inhibitors), and blockers of the receptors responsible for platelet aggregation. We anticipate that these will hasten the course of **thrombolysis** and limit the rates of reocclusion and reinfarction. Although a consensus has not yet developed concerning the optimal available agent, we have a steadily increasing armamentarium of both **thrombolytic** and adjunctive agents that have proved most effective in reducing the morbidity and mortality associated with acute myocardial infarction.

REFERENCES:

[1] Chesebro JH, TIMI principal investigators. **Thrombolysis** in Myocardial Infarction (TIMI) trial, phase I: a comparison between **intravenous** tissue plasminogen activator and **intravenous** streptokinase. Circulation. 1987;76:142-154.

[2] Verstraete M, Bernard R, Bory M, et al. Randomized trial of **intravenous** recombinant tissue-type plasminogen activator versus **intravenous** streptokinase in acute myocardial infarction. Lancet. 1985; 1:842-847.

[3] Tiefenbrunn AJ, Sobel BE. The impact of **coronary thrombolysis** on myocardial infarction. Fibrinolysis. 1989;3:1-15.

[4] Anderson JL, Rothbard RL, Hackworthy RA, et al. Multicenter reperfusion trial of **intravenous** anisolayted plasminogen streptokinase activator complex (APSAC) in acute myocardial infarction: controlled comparison with intracoronary streptokinase...

...Hogg K, Gemill J, Lifson K, et al. Comparative effects of anistreplase and streptokinase on **coronary artery** patency in acute myocardial infarction. Circulation. 1989:80(suppl IV):1667. Abstract.

[6] Bassand JP...

...Coll Cardiol. 1989;13:988-997.

[7] Mueller HS, Rao AK, Forman SA, TIMI investigators. **Thrombolysis** in Myocardial Infarction (TIMI): comparative studies of **coronary** reperfusion and systemic fibrinogenolysis with two forms of recombinant tissue-type plasminogen activator. J Am...

...479-490.

[8] TIMI Study Group. Comparison of invasive and conservative strategies after treatment with **intravenous** tissue plasminogen activator in acute myocardial infarction. Results of the **Thrombolysis** in Myocardial Infarction (TIMI) phase II trial. N Engl J Med. 1989;230:618-627.

[9] Magnani B. Plasminogen Activator Italian Multicenter Study (PAIMS): comparison of **intravenous** recombinant single-chain human tissue-type plasminogen activator (rt-PA) with **intravenous** streptokinase in acute ...1989;13:19-26.

[10] White HD, Rivers JT, Maslowski AH, et al. Effect of **intravenous** streptokinase as compared with that of tissue plasminogen activator on left ventricular function after first...

...J Med. 1989;320:817-821.

[11] Rao AK, Pratt C, Berke a, et al. **Thrombolysis** in Myocardial Infarction (TIMI) trial--phase I: hemorrhagic manifestations and changes in plasma fibrinogen and...

...II.

[12] Gruppo Italiano per lo Studio dell Streptochinasi nell'Infarto Miocardio (GISSI). Effectiveness of **intravenous** **thrombolytic** treatment in acute myocardial infarction. Lancet. 1986;1:397-401.

[13] Topol EJ, Califf RM, George BS, et al. The **Thrombolysis** and **Angioplasty** in Myocardial Infarction (TAMI) Study Group. A randomized trial of immediate versus delayed elective **angioplasty** after **intravenous** tissue plasminogen activator in acute myocardial infarction. N Engl J Med. 1987;317:581-588...

...Califf RM, Topol EJ, George BS, et al. TAMI 5: a randomized trial of combination **thrombolytic** therapy and immediate cardiac catherization. Circulation. 1989;80(suppl IV):1660. Abstract.

[15] Grines CL, Nissen SE, Booth DC. A new **thrombolytic** regimen for acute myocardial infarction using combination half-dose tissue plasminogen activator with full-dose...

...573-580.

[16] Second International Study of Infarction Survival (ISIS) Collaborative Group. Randomised trial of **intravenous** streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction...

...tissue plasminogen activator for mortality reduction in acute myocardial infarction, Anglo-Scandinavian Study of Early **Thrombolysis** (ASSET). Lancet. 1988;2:525-530.

[18] The APSAC Intervention Mortality Study (AIMS) Group. Effect of **intravenous** APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial. Lancet. 1988;1:545-549.

[19] Neuhaus K-L, Tebbe U, Gottwik M, et al. **Intravenous** recombinant tissue plasminogen activator (rt-PA) and urokinase in acute myocardial infarction: results of the...
...1988;12:581-587.

[20] Loscalzo J, Wharton TP, Kirshenbaum JM, et al. Clot-selective **coronary** **thrombolysis** with pro-urokinase. Circulation. 1989;79:776-782.

[21] Diefenbach C, Erbel R, Pop T...

...infarction. Am J Cardiol. 1988;61:966-970.

[22] Collen D, van de Werf F. **Coronary** **arterial** **thrombolysis** with low-dose synergistic combinations of recombinant single-chain urokinase-type plasminogen activator (rscu-PA...

...of medicine, section of cardiology, Baylor College of Medicine, and assistant director of the cardiac **catheterization** laboratory at The Methodist Hospital, Houston, Texas. Dr Pratt is associate professor of medicine and...

...DESCRIPTORS: **Thrombolytic** drugs

19900200

39/5,K/45 (Item 4 from file: 621)
DIALOG(R)File 621:Gale Group New Prod.Annou.(R)

01274179 Supplier Number: 45090165 (THIS IS THE FULLTEXT)
LOCALMED RECEIVES FDA APPROVAL TO MARKET THE INFUSASLEEVE CORONARY DRUG DELIVERY CATHETER
PR Newswire, pN/A
Oct 26, 1994
Language: English Record Type: Fulltext
Document Type: Newswire; Trade
Word Count: 441
TEXT:
LOCALMED RECEIVES FDA APPROVAL TO MARKET THE INFUSASLEEVE **CORONARY DRUG DELIVERY CATHETER**

PALO ALTO, CA., Oct. 26 /PRNewswire/ -- LocalMed, Inc., announced today that it has received FDA approval to market the Kaplan-Simpson InfusaSleeve(TM), a **catheter** which delivers medication directly to the **coronary artery** during **angioplasty** .

With more than a third of the world's 700,000 **angioplasty** patients requiring a second procedure within six months, the quest for a drug that prevents **restenosis** has been the industry's holy grail. Nearly fifty pharmaceutical and biotechnology firms are developing agents from simple heparin derivatives to high-tech antisense oligonucleotides in the hope that they will have some impact on this persistent problem. Available anti- **thrombotic** drugs like heparin, and direct **thrombin** inhibitors now under investigation, could also be very effective in reducing the risk of abrupt vessel closure in **angioplasty** after acute myocardial infarction. In all cases, though, the trick lies in **delivering** the **drug** to the injured segment of the **coronary artery** .

LocalMed believes it has the answer. Using its patented, over-the- **balloon** technology, the Palo Alto company has developed an infusion sleeve which tracks over virtually any **angioplasty balloon** and can deliver medication directly to the **angioplasty** site. The **InfusaSleeve** (TM) uses the existing **balloon** to position its **drug delivery** ports against the **artery** wall, permitting a precise fit within the **artery** and independent control of **drug infusion** , which the company believes is crucial for safe and effective local delivery.

This independent control is unique to LocalMed's approach and, if ongoing preclinical and clinical studies are any indication, they may be right. "Our preclinical trials demonstrated remarkable **drug delivery** efficiency with almost no injury," said Paul Goeld, LocalMed's CEO, "but our biggest advantages are flexibility and low cost. **Drugs** can be **infused** at virtually any pressure, **flow rate** or volume. It's safe, effective and easy to use." The company is currently planning a worldwide product launch.

Clinical use of the InfusaSleeve(TM) includes approximately fifty patients in Frankfurt, Germany and Milan, Italy. The device has been used in combination with most popular **angioplasty balloon catheters** and with three commercially available **coronary** stents. In addition, LocalMed is a collaborative partner in several investigations requiring intramural (**arterial** wall) delivery.

LocalMed is a private, venture-backed company. Its investors include Brentwood Associates, Burr, Egan, Deleage & Company, New Enterprise Associates, Three Arch Partners, OnSet Enterprise Associates, and Schroder Ventures.

The idea for the InfusaSleeve(TM) was developed by Aaron Kaplan, MD, while he was an interventional cardiologist at Stanford

University. Kaplan founded the company with the help of John Simpson and Thomas Fogarty, who have an enviable record of picking winners. LocalMed may be their biggest winner yet.

PUBLISHER NAME: PR Newswire Association, Inc.
COMPANY NAMES: *LocalMed
EVENT NAMES: *330 (Product information)
GEOGRAPHIC NAMES: *1U9CA (California); 1USA (United States)
PRODUCT NAMES: 2834030 (**Drug Delivery** Systems); 3842242 (Therapeutic **Balloon Catheters**)
INDUSTRY NAMES: BUS (Business, General); BUSN (Any type of business)
NAICS CODES: 325412 (Pharmaceutical Preparation Manufacturing); 339113 (Surgical Appliance and Supplies Manufacturing)
TRADE NAMES: InfusaSleeve

LOCALMED RECEIVES FDA APPROVAL TO MARKET THE INFUSASLEEVE CORONARY DRUG DELIVERY CATHETER

CORONARY DRUG DELIVERY CATHETER

PALO ALTO, CA., Oct. 26 /PRNewswire/ -- LocalMed, Inc., announced today that it has received FDA approval to market the Kaplan-Simpson InfusaSleeve(TM), a **catheter** which delivers medication directly to the **coronary artery** during **angioplasty** .

With more than a third of the world's 700,000 **angioplasty** patients requiring a second procedure within six months, the quest for a drug that prevents **restenosis** has been the industry's holy grail. Nearly fifty pharmaceutical and biotechnology firms are developing...

...in the hope that they will have some impact on this persistent problem. Available anti- **thrombotic** drugs like heparin, and direct **thrombin** inhibitors now under investigation, could also be very effective in reducing the risk of abrupt vessel closure in **angioplasty** after acute myocardial infarction. In all cases, though, the trick lies in **delivering** the **drug** to the injured segment of the **coronary artery** .

LocalMed believes it has the answer. Using its patented, over-the- **balloon** technology, the Palo Alto company has developed an infusion sleeve which tracks over virtually any **angioplasty balloon** and can deliver medication directly to the **angioplasty** site. The **InfusaSleeve** (TM) uses the existing **balloon** to position its **drug delivery** ports against the **artery** wall, permitting a precise fit within the **artery** and independent control of **drug infusion** , which the company believes is crucial for safe and effective local delivery.

This independent control...

...and clinical studies are any indication, they may be right. "Our preclinical trials demonstrated remarkable **drug delivery** efficiency with almost no injury," said Paul Goeld, LocalMed's CEO, "but our biggest advantages are flexibility and low cost. **Drugs** can be **infused** at virtually any pressure, **flow rate** or volume. It's safe, effective and easy to use." The company is currently planning...

...Frankfurt, Germany and Milan, Italy. The device has been used in combination with most popular **angioplasty balloon catheters** and with three commercially available **coronary** stents. In addition, LocalMed is a collaborative partner in several investigations requiring intramural (**arterial** wall) delivery.

LocalMed is a private, venture-backed company. Its investors include Brentwood Associates, Burr...

PRODUCT NAMES: 2834030 (**Drug Delivery** Systems); 3842242

(Therapeutic **Balloon Catheters**)
19941026

39/5,K/48 (Item 3 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00116189

Medical Progress: Advances in Coronary Angioplasty **(Review Article)**

Bittl, John A.
The New England Journal of Medicine
Oct 24, **1996** ; 335 (17),pp 1290-1302
LINE COUNT: 00560 WORD COUNT: 07740
ISSN: 0028-4793
CORPORATE SOURCE: From the Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston. Address reprint requests to Dr. Bittl at the Cardiovascular Division, Brigham and Women's Hospital, Boston, MA 02115.

CITED REFERENCES
1. Ellis SG, Omoigui N, Bittl JA, et al. Analysis and comparison of operator-specific outcomes in interventional cardiology: from a multicenter database of 4860 quality-controlled procedures. Circulation 1996;93:431-9.
2. Wolfe MW, Roubin GS, Schweiger M, et al. Length of hospital stay and complications after percutaneous transluminal **coronary angioplasty** : clinical and procedural predictors. Circulation 1995;92:311-9.
3. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of directional atherectomy with **coronary angioplasty** in patients with **coronary artery** disease. N Engl J Med 1993;329:221-7.
4. Adelman AG, Cohen EA, Kimball BP, et al. A comparison of directional atherectomy with **balloon angioplasty** for lesions of the left anterior descending **coronary artery** . N Engl J Med 1993;329:228-33.
5. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of **balloon** -expandable-stent implantation with **balloon angioplasty** in patients with **coronary artery** disease. N Engl J Med 1994;331:489-95.
6. Fischman DL, Leon MB, Baim DS, et al. A randomized comparison of **coronary** -stent placement and **balloon angioplasty** in the treatment of **coronary artery** disease. N Engl J Med 1994;331:496-501.
7. Ellis SG, Cowley MJ, Whitlow PL, et al. Prospective case-control comparison of percutaneous transluminal **coronary** revascularization in patients with multivessel disease treated in 1986-1987 versus 1991: improved in-hospital and 12-month results. J Am Coll Cardiol 1995;25:1137-42.
8. Detre K, Holubkov R, Kelsey S, et al. Percutaneous transluminal **coronary angioplasty** in 1985-1986 and 1977-1981: the National Heart, Lung, and Blood Institute Registry. N Engl J Med 1988;318:265-70.
9. Nobuyoshi M, Kimura T, Nosaka H, et al. **Restenosis** after successful percutaneous transluminal **coronary angioplasty** : serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616-23.
10. The EPIC Investigators. Use of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk **coronary angioplasty** . N Engl J Med 1994;330:956-61.
11. Topol EJ, Califf RM, Weisman HF, et al. Randomised trial of **coronary** intervention with antibody against platelet IIb/IIIa integrin for reduction of clinical **restenosis** : results at six months. Lancet 1994;343:881-6.
12. Topol EJ. Evaluation of PTCA to Improve Long-Term Outcomes with c7E3 Glycoprotein IIb/IIIa-Receptor Blockade (EPILOG). Presented at the Scientific Sessions of the European Society of Cardiology, Birmingham, England, August 27, 1996.
13. Landau C, Lange RA, Hillis LD. Percutaneous transluminal **coronary angioplasty** . N Engl J Med 1994;330:981-93.
14. Lemaitre DT, Barber AP, Mullen MG. Interventional cardiology. The Cowen

Report. March 6, 1996:1-32.
15. Kuntz RE, Gibson CM, Nobuyoshi M, Baim DS. Generalized model of **restenosis** after conventional **balloon angioplasty** , stenting and directional atherectomy. J Am Coll Cardiol 1993;21:15-25.
16. Roubin GS, Douglas JS Jr, King SB III, et al. Influence of **balloon** size on initial success, acute complications, and **restenosis** after percutaneous transluminal **coronary angioplasty** : a prospective randomized study. Circulation 1988;78:557-65.
17. Holmes DR Jr, Topol EJ, Califf RM, et al. A multicenter, randomized trial of **coronary angioplasty** versus directional atherectomy for patients with saphenous **vein** bypass graft lesions: CAVEAT-II Investigators. Circulation 1995;91:1966-74.
18. Appelman YEA, Piek JJ, Strikwerda S, et al. Randomised trial of excimer laser **angioplasty** versus **balloon angioplasty** for treatment of **obstructive coronary artery** disease. Lancet 1996;347:79-84.
19. Appelman YEA, Koolen JJ, Piek JJ, et al. Excimer laser **angioplasty** versus **balloon angioplasty** in functional and total **coronary occlusions** . Am J Cardiol 1996;78:757-62.
20. Bittl JA. Directional **coronary** atherectomy versus **balloon angioplasty** . N Engl J Med 1993;329:273-4.
21. Harrington RA, Lincoff AM, Califf RM, et al. Characteristics and consequences of myocardial infarction after percutaneous **coronary** intervention: insights from the **Coronary Angioplasty** Versus Excisional Atherectomy Trial (CAVEAT). J Am Coll Cardiol 1995;25:1693-9.
22. Elliott JM, Berdan LG, Holmes DR, et al. One-year follow-up in the **Coronary Angioplasty** Versus Excisional Atherectomy Trial (CAVEAT I). Circulation 1995;91:2158-66.
23. Baim DS, Simonton CA, Popma JJ, et al. Mechanism of **lumen** enlargement by optimal a therectomy -- IVUS insights from the OARS Study. J Am Coll Cardiol 1996;27:Suppl A:291A. abstract.
24. Mintz GS, Kovach JA, Javier SP, et al. Mechanisms of **lumen** enlargement after excimer laser **coronary angioplasty** : an **intravascular** ultrasound study. Circulation 1995;92:3408-14.
25. Baumbach A, Bittl JA, Fleck E, et al. Acute complications of excimer laser **coronary angioplasty** : a detailed analysis of multicenter results. J Am Coll Cardiol 1994;23:1305-13.
26. Bittl JA, Ryan TJ Jr, Keaney JF Jr, et al. **Coronary artery** perforation during excimer laser **coronary angioplasty** . J Am Coll Cardiol 1993;21:1158-65.
27. van Leeuwen TG, Meertens JH, Velema E, Post MJ, Borst C. Intraluminal vapor bubble induced by excimer laser pulse causes microsecond **arterial** dilation and invagination leading to extensive wall damage in the rabbit. Circulation 1993;87:1258-63.
28. Deckelbaum LI, Natarajan MK, Bittl JA, et al. Effect of intracoronary saline infusion on dissection during excimer laser **coronary angioplasty** : a randomized trial. J Am Coll Cardiol 1995;26:1264-9.
29. Safian RD, Niazi KA, Strzelecki M, et al. Detailed angiographic analysis of high-speed mechanical rotational atherectomy in human **coronary arteries** . Circulation 1993;88:961-8.
30. MacIsaac AI, Bass TA, Buchbinder M, et al. High speed rotational atherectomy: outcome in calcified and noncalcified **coronary artery** lesions. J Am Coll Cardiol 1995;26:731-6.
31. Vandormael M, Reifart N, Preusler W, et al. Six months follow-up results following excimer laser **angioplasty** , rotational atherectomy and **balloon angioplasty** for complex lesions: ERBAC Study. Circulation 1994;90:Suppl:I-213. abstract.
32. de Muinck ED, den Heijer P, van Dijk RB, et al. Autoperfusion **balloon** versus stent for acute or threatened closure during percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1994;74:1002-5.
33. Lincoff AM, Topol EJ, Chapekis AT, et al. Intracoronary stenting compared with conventional therapy for abrupt vessel closure complicating **coronary angioplasty** : a matched case-control study. J Am Coll Cardiol 1993;21:866-75.
34. Roubin GS, Cannon AD, Agrawal SK, et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal **coronary angioplasty** . Circulation 1992;85:916-27.
35. Lincoff AM, Popma JJ, Ellis SG, Hacker JA, Topol EJ. Abrupt vessel

closure complicating **coronary angioplasty** : clinical, angiographic and therapeutic profile. J Am Coll Cardiol 1992;19:926-35.
36. White CJ, Ramee SR, Collins TJ, Jain SP, Escobar A. **Coronary** angioscopy of abrupt **occlusion** after **angioplasty** . J Am Coll Cardiol 1995;25:1681-4.
37. Sutton JM, Ellis SG, Roubin GS, et al. Major clinical events after **coronary** stenting: the multicenter registry of acute and elective Gianturco-Roubin stent placement. Circulation 1994;89:1126-37.
38. Hasdai D, Garratt KN, Holmes DR Jr, Berger PB, Schwartz RS, Bell MR. **Coronary angioplasty** and intracoronary **thrombolytics** are of limited efficacy in resolving early intracoronary stent **thrombosis** . J Am Coll Cardiol 1996;28:361-7.
39. Macaya C, Serruys PW, Ruygrok P, et al. Continued benefit of **coronary** stenting versus **balloon angioplasty** : one-year clinical follow-up of Benestent trial. J Am Coll Cardiol 1996;27:255-61.
40. Kimura T, Yokoi H, Nakagawa Y, et al. Three-year follow-up after implantation of metallic **coronary - artery** stents. N Engl J Med 1996;334:561-6.
41. Itoh A, Colombo A, Hall P, et al. Stenting in protected and unprotected left main **coronary artery** : immediate and follow-up results. J Am Coll Cardiol 1996;27:Suppl A:277A. abstract.
42. Piana RN, Moscucci M, Cohen DJ, et al. Palmaz-Schatz stenting for treatment of focal **vein** graft **stenosis** : immediate results and long-term outcome. J Am Coll Cardiol 1994;23:1296-304.
43. Wong SC, Baim DS, Schatz RS, et al. Immediate results and late outcomes after stent implantation in saphenous **vein** graft lesions: the multicenter U.S. Palmaz-Schatz stent experience. J Am Coll Cardiol 1995;26:704-12.
44. Goldberg SL, Colombo A, Maiello L, Borrione M, Finci L, Almagor Y. Intracoronary stent insertion after **balloon angioplasty** of chronic total **occlusions** . J Am Coll Cardiol 1995;26:713-9.
45. Serruys PW, Leon M, Hamburger JN, et al. Recanalization of chronic total **coronary occlusions** using a laser guide wire: the EU and US TOTAL experience. J Am Coll Cardiol 1996;27:Suppl A:152A. abstract.
46. Popma JJ, Coller BS, Ohman EM, et al. Antithrombotic therapy in patients undergoing **coronary angioplasty** . Chest 1995;108:Suppl:486S-501S.
47. Mak K-H, Belli G, Ellis SG, Moliterno DJ. Subacute stent **thrombosis** : evolving issues and current concepts. J Am Coll Cardiol 1996;27:494-503.
48. Bittl JA. Subacute stent **occlusion** : **thrombus** horribilis. J Am Coll Cardiol 1996;28:368-70.
49. Colombo A, Hall P, Nakamura S, et al. Intracoronary stenting without anticoagulation accomplished with **intravascular** ultrasound guidance. Circulation 1995;91:1676-88.
50. Neumann F-J, Gawaz M, Ott I, May A, Mossmer G, Schomig A. Prospective evaluation of hemostatic predictors of subacute stent **thrombosis** after **coronary** Palmaz-Schatz stenting. J Am Coll Cardiol 1996;27:15-21.
51. Schomig A, Neumann F-J, Kastrati A, et al. A randomized comparison of antiplatelet and anticoagulation therapy after the placement of **coronary - artery** stents. N Engl J Med 1996;334:1084-9.
52. Serruys PW, Emanuelsson H, van der Giessen W, et al. Heparin-coated Palmaz-Schatz stents in human **coronary arteries** : early outcome of the Benestent-II Pilot Study. Circulation 1996;93:412-22.
53. Rogers C, Edelman ER. Endovascular stent design dictates experimental **restenosis** and **thrombosis** . Circulation 1995;91:2995-3001.
54. Currier JW, Faxon DP. **Restenosis** after percutaneous transluminal **coronary angioplasty** : have we been aiming at the wrong target? J Am Coll Cardiol 1995;25:516-20.
55. O'Brien ER, Alpers CE, Stewart DK, et al. Proliferation in primary and **restenotic coronary** atherectomy tissue: implications for antiproliferative therapy. Circ Res 1993;73:223-31.
56. Mintz GS, Popma JJ, Pichard AD, et al. **Intravascular** ultrasound predictors of **restenosis** after percutaneous transcatheter **coronary** revascularization. J Am Coll Cardiol 1996;27:1678-87.
57. Mintz GS, Popma JJ, Pichard AD, et al. **Arterial** remodeling after **coronary angioplasty** : a serial **intravascular** ultrasound study.

Circulation 1996;94:35-43.
58. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic **coronary arteries** . N Engl J Med 1987;316:1371-5.
59. Kakuta T, Currier JW, Haudenschild **CC** , Ryan TJ, Faxon DP. Differences in compensatory vessel enlargement, not intimal formation, account for **restenosis** after **angioplasty** in the hypercholesterolemic rabbit model. Circulation 1994;89:2809-15.
60. Strauss BH, Chisholm RJ, Keeley FW, Gotlieb AI, Logan RA, Armstrong PW. Extracellular matrix remodeling after **balloon angioplasty** injury in a rabbit model of **restenosis** . Circ Res 1994;75:650-8.
61. Dussaillant GR, Mintz GS, Pichard AD, et al. Small stent size and intimal hyperplasia contribute to **restenosis** : a volumetric **intravascular** ultrasound analysis. J Am Coll Cardiol 1995;26:720-4.
62. Fernandez-Ortiz A, Badimon JJ, Falk E, et al. Characterization of the relative **thrombogenicity** of atherosclerotic **plaque** components: implications for consequences of **plaque** rupture. J Am Coll Cardiol 1994;23:1562-9.
63. Merino A, Cohen M, Badimon JJ, Fuster V, Badimon L. Synergistic action of severe wall injury and shear forces on **thrombus** formation in **arterial stenosis** : definition of a **thrombotic** shear rate threshold. J Am Coll Cardiol 1994;24:1091-7.
64. Marmur JD, Merlini PA, Sharma SK, et al. **Thrombin** generation in human **coronary arteries** after percutaneous transluminal **balloon angioplasty** . J Am Coll Cardiol 1994;24:1484-91.
65. Coughlin SR, Vu TK, Hung DT, Wheaton VI. Characterization of a functional **thrombin** receptor: issues and opportunities. J Clin Invest 1992;89:351-5.
66. Hirsh J, Fuster V. Guide to anticoagulant therapy. I. Heparin. Circulation 1994;89:1449-68.
67. Serruys PW, Herrman J-PR, Simon R, et al. A comparison of hirudin with heparin in the prevention of **restenosis** after **coronary angioplasty** . N Engl J Med 1995;333:757-63.
68. Bittl JA, Strony J, Brinker JA, et al. Treatment with bivalirudin (Hirulog) as compared with heparin during **coronary angioplasty** for unstable or postinfarction angina. N Engl J Med 1995;333:764-9.
69. Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of **coronary artery** disease and the acute **coronary** syndromes. N Engl J Med 1992;326:242-50, 310-8.
70. Tcheng JE, Lincoff AM, Sigmon KN, Califf RM, Topol EJ. Platelet glycoprotein IIb/IIIa inhibition with Integrelin during percutaneous **coronary** intervention: the IMPACT II Trial. Circulation 1995;92:Suppl I:I-543. abstract.
71. Horrigan MCG, Tcheng JE, Califf RM, et al. Maximal benefit of Integrelin platelet IIb/IIIa blockade 6-12 hours after therapy: results of the IMPACT-II Trial. J Am Coll Cardiol 1996;27:Suppl A:55A. abstract.
72. Ambrose JA, Almeida OD, Sharma SK, et al. Adjunctive **thrombolytic** therapy during **angioplasty** for **ischemic** rest angina: results of the TAUSA Trial. Circulation 1994;90:69-77.
73. The TIMI IIIB Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction: results of the TIMI IIIB Trial. Circulation 1994;89:1545-56.
74. Eisenberg PR, Sobel BE, Jaffe AS. Activation of prothrombin accompanying **thrombolysis** with recombinant tissue-type plasminogen activator. J Am Coll Cardiol 1992;19:1065-9.
75. Parisi AF, Folland ED, Hartigan P. A comparison of **angioplasty** with medical therapy in the treatment of single-vessel **coronary artery** disease. N Engl J Med 1992;326:10-6.
76. Hueb WA, Bellotti G, de Oliveira SA, et al. The Medicine, **Angioplasty** , or Surgery Study (MASS): a prospective, randomized trial of medical therapy, **balloon angioplasty** or bypass surgery for single proximal left anterior descending **artery stenoses** . J Am Coll Cardiol 1995;26:1600-5.
77. Anderson HV, Cannon CP, Stone PH, et al. One-year results of the **Thrombolysis** in Myocardial Infarction (TIMI) IIIB clinical trial: a randomized comparison of tissue-type plasminogen activator versus

placebo and early invasive versus early conservative strategies in unstable angina and non-Q wave myocardial infarction. J Am Coll Cardiol 1995;26:1643-50.
78. Michels KB, Yusuf S. Does PTCA in acute myocardial infarction affect mortality and reinfarction rates? A quantitative overview (meta-analysis) of the randomized clinical trials. Circulation 1995;91:476-85.
79. Every NR, Parsons LS, Hlatky M, Martin JS, Weaver WD. A comparison of **thrombolytic** therapy with primary **coronary angioplasty** for acute myocardial infarction. N Engl J Med 1996;335:1253-60.
80. Pocock SJ, Henderson RA, Rickards AF, et al. Meta-analysis of randomised trials comparing **coronary angioplasty** with bypass surgery. Lancet 1995;346:1184-9.
81. The Bypass **Angioplasty** Revascularization Investigation (BARI) Investigators. Comparison of **coronary** bypass surgery with **angioplasty** in patients with multivessel disease. N Engl J Med 1996;335:217-25.
82. Hamm CW, Reimers J, Ischinger T, Rupprecht H-J, Berger J, Bleifield W. A randomized study of **coronary angioplasty** compared with bypass surgery in patients with symptomatic multivessel **coronary** disease. N Engl J Med 1994;331:1037-43.
83. King SB III, Lembo NJ, Weintraub WS, et al. A randomized trial comparing **coronary angioplasty** with **coronary** bypass surgery. N Engl J Med 1994;331:1044-50.
84. RITA Trial Participants. **Coronary angioplasty** versus **coronary artery** bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. Lancet 1993;341:573-80.
85. Aronson D, Bloomgarden Z, Rayfield EJ. Potential mechanisms promoting **restenosis** in diabetic patients. J Am Coll Cardiol 1996;27:528-35.
86. Brown G, Albers JJ, Fisher LD, et al. Regression of **coronary artery** disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B. N Engl J Med 1990;323:1289-98.
87. Weintraub WS, Boccuzzi SJ, Klein JL, et al. Lack of effect of lovastatin on **restenosis** after **coronary angioplasty** . N Engl J Med 1994;331:1331-7.
88. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with **coronary** heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383-9.
89. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on **coronary** events after myocardial infarction in patients with average cholesterol levels. N Engl J Med 1996;335:1001-9.
90. Treasure CB, Klein JL, Weintraub WS, et al. Beneficial effects of cholesterol-lowering therapy on the **coronary** endothelium in patients with **coronary artery** disease. N Engl J Med 1995;332:481-7.
91. Anderson TJ, Meredith IT, Yeung AC, Frei B, Selwyn AP, Ganz P. The effect of cholesterol-lowering and antioxidant therapy on endothelium-dependent **coronary** vasomotion. N Engl J Med 1995;332:488-93.
92. Ambrose JA, Tannenbaum MA, Alexopoulos D, et al. Angiographic progression of **coronary artery** disease and the development of myocardial infarction. J Am Coll Cardiol 1988;12:56-62.
93. Little WC, Constantinescu M, Applegate RJ, et al. Can **coronary** angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate **coronary artery** disease? Circulation 1988;78:1157-66.
94. Uren NG, Melin JA, De Bruyne B, Wijns W, Baudhuin T, Camici PG. Relation between myocardial blood flow and the severity of **coronary - artery stenosis** . N Engl J Med 1994;330:1782-8.
95. Mintz GS, Painter JA, Pichard AD, et al. Atherosclerosis in angiographically ``normal'' **coronary artery** reference segments: an **intravascular** ultrasound study with clinical correlations. J Am Coll Cardiol 1995;25:1479-85.
96. Topol EJ, Nissen SE. Our preoccupation with **coronary** luminology: the dissociation between clinical and angiographic findings in **ischemic** heart disease. Circulation 1995;92:2333-42.
97. The GUIDE Trial Investigators. IVUS-determined predictors of **restenosis** in PTCA and DCA: final report from the GUIDE Trial, Phase

II. J Am Coll Cardiol 1996;27:Suppl A:156A. abstract.
* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

Medical Progress: Advances in Coronary Angioplasty **(Review Article)**
1996 ;

TEXT
...The goal of therapy in patients with **coronary artery** disease is to alleviate symptoms of angina and reduce the risk of death or nonfatal myocardial infarction. Although **coronary angioplasty** immediately reduces anginal symptoms in almost all patients who undergo it, its use is associated...

...or nonfatal myocardial infarction in about 5 percent of patients (Ref. 1-8) and with **restenosis** requiring repeated **angioplasty** or bypass surgery in about 30 percent. (Ref. 3-6,9) Recently, several clinical trials have shown that the implantation of **coronary** stents (Ref. 5,6) or treatment with blockers of platelet glycoprotein IIb/IIIa receptors (Ref. 10-12) reduces the occurrence of acute complications and **restenosis** in patients undergoing **coronary angioplasty** . These new therapies have spread rapidly and have changed the practice of interventional cardiology remarkably...

...Advances in **coronary angioplasty** have not occurred in isolation. There have also been improvements in the medical and surgical treatment of **coronary artery** disease, along with new insights into the natural history of **coronary** atherosclerosis. An update on **coronary angioplasty** is thus incomplete without attention to the benefits of new medical and surgical therapies. The...

...Devices for **Coronary** Revascularization
The growth of interventional cardiovascular procedures has been staggering (Fig. 1). Almost 900,000 **coronary angioplasty** procedures were performed worldwide in 1995. (Ref. 14) Since 1994, the use of **balloon angioplasty** has leveled off, while the use of **coronary** stents has grown substantially. The number of stent-implantation procedures is expected to exceed that of conventional **balloon angioplasty** procedures by the year 2000. (Ref. 14)|*Figure 1.-Rate of Growth in the Use...

...rates for 1996 are estimates. Data are from Lemaitre et al. (Ref. 14).**FIGURE OMITTED**
Balloon Angioplasty
Balloon catheters are used as the sole devices in percutaneous transluminal **coronary angioplasty** (PTCA), or `` **balloon angioplasty** ,'' and as adjunctive dilating devices in most other interventional procedures. Since 1994, **balloon catheters** have undergone technical refinements. The deflated profile of 3.0-mm **balloon catheters** has been reduced from 0.037 in. (0.94 mm) to about 0.030 in. (0.76 mm). Improvements in **catheter** design have been partially responsible for higher success rates in recent years despite the older age of the patients and the more frequent occurrence of unstable angina and multivessel **coronary artery** disease in patients undergoing PTCA than in the past (Table 1).|*Table 1.-Increasing Success...

...Although the efficacy of PTCA has improved, it does not consistently result in a large **lumen** in the dilated vessel. This is important, because **arteries** with larger **lumen** diameters have a lower risk of subsequent **restenosis** than incompletely dilated **arteries** (the observation being that ``bigger is better''). (Ref. 15) When oversized **balloons** are used to dilate **coronary** vessels, however, the risk of vessel dissection and **ischemic** complications increases. (Ref. 16) Thus, several approaches involving the removal of atheromatous tissue have been developed to overcome the limitations of PTCA.
Atherectomy and Laser **Angioplasty**
During directional **coronary** atherectomy, atherosclerotic tissue is extracted from the **coronary artery** with a cutting blade spinning at 5000 rpm in the tip of the atherectomy device. During excimer-laser **angioplasty** , light at a wavelength of 308 nm emitted from optical fibers

at the **catheter** tip vaporizes atheromatous tissue. Although directional atherectomy and excimer-laser **angioplasty** usually result in larger **lumen** diameters than PTCA, these new treatments have not reduced the rates of acute complications or **restenosis** after **coronary** **angioplasty** . (Ref. 3,4,17-19) Some investigators have attributed the failure of directional atherectomy to...

...the fact that conservative cutting techniques have produced only a moderate increase in the final **lumen** diameter. (Ref. 20...The failure of excimer-laser **angioplasty** to achieve better clinical outcomes than PTCA was also attributed to inadequate tissue removal, (Ref...

...Ref. 27) The incidence of dissection may be reduced by infusing saline through the guide **catheter** during excimer-laser **angioplasty** . (Ref. 28 ...

...Rotational atherectomy (Ref. 29,30) is another approach for removing atheromatous **plaque** from **coronary** **arteries** . This technique uses a diamond-studded burr spinning at about 180,000 rpm to excavate calcified or fibrotic **plaque** , allowing microscopic debris to embolize to the **coronary** capillary bed. No multicenter, randomized trials proving its superiority over PTCA have been reported. The Excimer Laser Rotational Atherectomy **Balloon** **Angioplasty** Comparison was a single-center study involving 615 patients who underwent rotational atherectomy, excimer-laser **angioplasty** , or PTCA. (Ref. 31) Although rotational atherectomy was associated with a higher short-term success rate than PTCA (90 percent vs. 80 percent), the rates of major **ischemic** complications or repeated revascularization were higher six months after treatment (46 percent vs. 37 percent). (Ref. 31)

Coronary Stenting

Coronary stents are fenestrated stainless-steel tubes that can be expanded by a **balloon** and provide a scaffold within **coronary** **arteries** to treat acute vessel dissection and reduce the risk of **restenosis** . Two designs are currently approved by the Food and **Drug** **Administration** for general use (Fig. 2).|*Figure 2.- **Coronary** Stents Approved for Use by the Food and **Drug** **Administration** .Panel A shows a stainless-steel, slotted-tube, Palmaz-Schatz stent. An unexpanded stent is shown at the top of the panel, followed by an unexpanded stent mounted on a **balloon** **catheter** , an expanded stent on a fully dilated **balloon** , and an expanded stent with its slotted-tube configuration after deflation and removal of the **balloon** **catheter** . Although this stent is approved for use in reducing **restenosis** in native **coronary** **arteries** 3.0 mm or more in diameter, it is also widely used for other indications, such as abrupt vessel closure. Panel B shows **balloon** -expanded, stainless-steel, flexible-coil Gianturco-Roubin stents in 12-mm and 20-mm lengths...

...Current Applications

Coronary stenting reduces the immediate need for bypass surgery for abrupt vessel closure during PTCA. (Ref...

...appropriate, because this problem is predominantly caused by mechanical disruption, such as vessel dissection or **plaque** extrusion, in almost 80 percent of cases and by **thrombus** in about 20 percent of cases. (Ref. 2,35,36) When stenting is used to treat **thrombus** -containing lesions, however, the risk of **ischemic** complications increases. (Ref. 37,38...

... **Coronary** stenting also reduces the likelihood of **restenosis** in particular groups of patients. Two multicenter, randomized trials showed that the incidence of **restenosis** was 25 to 30 percent lower after **coronary** stenting than after PTCA for new lesions in large native **coronary** **arteries** measuring 3.0 mm or more in diameter (Table 2). (Ref. 5,6,39) Late **restenosis** of **coronary** stents is rare. The **lumen** diameter of stented **arteries** did not decrease, according to serial angiographic observations made from six months to three years...

...The use of **coronary** stents has not been restricted to the prevention of **restenosis** or the treatment of abrupt vessel closure. This versatile therapy is commonly used on a provisional basis for residual narrowings or mild dissections after PTCA. **Coronary** stenting is used in high-risk

situations unlikely to be successfully managed with conventional PTCA. For example, **coronary** stents are used to treat **stenoses** of the left main **coronary artery** in patients who cannot undergo bypass surgery (Fig. 3), (Ref. 41) **stenoses** in diseased saphenous- **vein** grafts, (Ref. 42,43) and total **occlusions** recanalized with PTCA or laser **angioplasty** . (Ref. 44,45)|*Figure 3.-Emergency Stenting for Threatened Closure of the Left Main **Coronary Artery** . **Restenosis** developed in a 77-year-old man 11 months after the implantation of a slotted-tube stent within the proximal segment of the left anterior descending **coronary artery** (Panel A, arrows). Attempts to dilate the segment were complicated by the formation of a dissection involving the distal left main **coronary artery** (Panel B, arrow). The dissection impaired flow into the left anterior descending (Panel B, arrowhead) and left circumflex **coronary arteries** and caused widespread myocardial **ischemia** with hypotension. Additional slotted-tube stents were placed in the left main **coronary artery** (Panel C, arrow) and the proximal left anterior descending **artery** (Panel C, arrowhead) across the origin of the left circumflex **coronary artery** , relieving **ischemia** and hypotension. Bypass surgery was not recommended because of the excellent angiographic result and the increased risk of surgery in this patient, who had severe chronic **obstructive** pulmonary disease and chronic muscle weakness from previous Guillain-Barre syndrome. Clinical evaluation at seven...

...Subacute **Thrombotic Occlusion** of **Coronary** Stents

The chief limitation of **coronary** stenting is subacute **thrombotic occlusion** , which occurs in about 4 percent of patients within 2 to 14 days after stent...

...always results in a myocardial infarction or death. (Ref. 5,6,38,46-48) Subacute **thrombotic occlusion** after stent implantation is a more serious problem than complete vessel closure after PTCA. The...

...percent of patients but appears most commonly while the patient is still in the cardiac **catheterization** laboratory, where the problem can be treated. Moreover, only one third of patients with complete vessel closure after PTCA have major **ischemic** complications. (Ref. 2...
...Initial efforts to prevent stent-associated **thrombosis** involved an intensive anticoagulation regimen consisting of aspirin, dipyridamole, dextran, and heparin during stent implantation and warfarin after the procedure. When bleeding and stent-associated **thrombosis** occurred simultaneously in some patients receiving anticoagulation therapy, it became clear that this approach did not prevent **thrombosis** . Using **intravascular** ultrasound imaging, Colombo and colleagues (Ref. 49) showed that stents must be dilated after implantation with **balloons** at high pressures (up to 16 to 20 atmospheres). When stents are fully expanded, the risk of subacute **thrombotic occlusion** is low, even in patients who are not receiving anticoagulation therapy. (Ref. 49) Because high-pressure **balloon inflations** are used in most cases to expand **coronary** stents, **intravascular** ultrasound imaging may not be needed routinely to document full stent expansion. In a pooled analysis, stent-associated **thrombosis** occurred in only 33 of 2630 patients (1.3 percent) who did not receive anticoagulation therapy; and more than two thirds of all patients did not undergo **intravascular** ultrasound imaging. (Ref. 47...

...that activation of platelets, rather than the coagulation pathway, increases the risk of stent-associated **thrombosis** . This observation was the basis for a randomized trial comparing the combination of ticlopidine and...
...the anticoagulant phenprocoumon and aspirin. The former regimen resulted in lower rates of stent-associated **thrombosis** (0.8 percent vs. 5.4 percent, P = 0.004) and major hemorrhage (0.0...

...under way to determine whether alternative antithrombotic approaches reduce the risk of major complications of **coronary** -stent implantation as compared with PTCA...

...Innovations in **Coronary** Stents

New stent designs, such as the heparin-coated stent evaluated in the

Belgium-Netherlands...

...may have important clinical benefits. (Ref. 52) There were no instances of documented stent-associated **thrombosis** in 207 consecutive patients, among whom 2.0 percent died, 1.5 percent had myocardial...

...percent needed bypass surgery, 1.5 percent had stroke, and 8.9 percent underwent repeated **angioplasty** within seven months after stent implantation for stable angina. This finding suggests that use of...

...design, implantation technique, and antithrombotic therapy in selected patients could reduce the rate of subacute **thrombotic occlusion** seen with bare metallic stents and anticoagulation with warfarin (Table 2... likely to have important clinical consequences. For example, an experimental study found lower rates of **thrombosis** and **lumen** narrowing with the use of a stainless-steel, corrugated-ring stent than with a stainless...

... **Coronary** Stenting and the Process of **Restenosis**

New concepts of **restenosis** have emerged simultaneously with the widespread use of **coronary** stents. Early studies suggested that intimal proliferation is the predominant cause of narrowing of the **lumen** after **arterial** injury in animals with normal or elevated cholesterol levels. On the basis of the results...

...enrolling more than 13,000 patients have evaluated various drugs to block intimal proliferation after **coronary angioplasty** , but none of the drugs have produced consistently beneficial results. (Ref. 54...

...Recent studies have challenged the proliferation model of **restenosis** . Using immunohistochemical labeling of proliferative-cell nuclear antigen in **restenotic** lesions extracted with directional atherectomy, O'Brien and colleagues (Ref. 55) found only scanty evidence of cellular proliferation and no obvious temporal peak during a six-month period after **angioplasty** . Mintz and colleagues (Ref. 56,57) used serial **intravascular** ultrasound imaging after various **coronary** interventions to quantify the separate contributions of vessel-wall geometry, atherosclerotic **plaque** , and the vessel **lumen** to the process of **restenosis** . They found that intimal thickening accounted for about 30 percent of the loss in **lumen** diameter six months after **coronary** interventions, whereas shrinkage of the dilated segment, measured as a reduction in the cross-sectional...

...Current studies thus suggest that **restenosis** is predominantly influenced by **arterial** remodeling -- a process that consists of either an adaptive increase or a pathologic shrinkage of...

...the vessel (Fig. 4). Whereas adaptive remodeling has been identified in the course of human **coronary** atherosclerosis as a mechanism that delays the development of focal **stenoses** in the presence of enlarging atheromas, (Ref. 58) pathologic remodeling has been observed as a process that increases the encroachment of atheroma and neointima on the **arterial lumen** , as was observed initially in studies of **restenosis** in rabbits. (Ref. 59,60)|*Figure 4.-Possible Mechanisms of **Restenosis** after PTCA and **Coronary** Stenting.Serial **intravascular** ultrasound studies suggest that PTCA almost always disrupts **plaque** without reducing the total intimal area, frequently causes dissections that penetrate into the tunica media... ...enlarges the vessel, measured as the cross-sectional area subtended by the external elastic lamina. **Restenosis** is caused by pathologic **arterial** remodeling, characterized by shrinkage of the area circumscribed by the external elastic lamina, and to a lesser extent by neointimal thickening. **Coronary** stenting also enlarges the cross-sectional area of the vessel. The radial force of the...

... **Coronary** stenting reduces the incidence of **restenosis** because it produces large **lumens** (Ref. 15) and staves off pathologic remodeling. (Ref. 61) Serial **intravascular** ultrasound studies suggest that neointimal proliferation through the stent struts accounts for almost all the late loss in **lumen** diameter after **coronary** stenting, with almost no evidence

of vessel shrinkage or collapse of the stent (Fig. 4...

...New Antithrombotic Therapies for use during **Coronary Angioplasty**
In 1994 the mainstay of anticoagulation therapy during PTCA was the combination of aspirin (325...

...The extent of **arterial - thrombus** formation during **coronary angioplasty** depends on the degree of platelet activation on exposure to **thrombogenic** components of atheromatous **plaques** (Ref. 62) and changes in shear caused by **stenoses** . (Ref. 63) **Thrombin** is generated during **coronary angioplasty** (Ref. 64) and potently activates platelets. (Ref. 65) Because heparin has several limitations as a **thrombin** inhibitor, including its requirement for cofactor antithrombin III and inhibition within platelet-rich **thrombi** , (Ref. 66) direct **thrombin** inhibitors have been developed as possible substitutes. Two multicenter studies (Ref. 67,68) evaluated the direct **thrombin** inhibitors hirudin and bivalirudin in patients undergoing PTCA for unstable angina and found that these agents were marginally better than heparin in preventing **ischemic** complications. The failure of direct **thrombin** inhibitors to show a striking advantage over heparin during **angioplasty** is now attributed to the multiplicity of pathways for platelet activation (Ref. 69) and the inability of these agents, unlike heparin, to block the generation of **thrombin** . (Ref. 67...

...the monoclonal antibody abciximab, or c7E3. In the Evaluation of Abciximab for the Prevention of **Ischemic** Complications (EPIC) study, (Ref. 10) 2099 patients undergoing PTCA or directional atherectomy for acute myocardial infarction, refractory unstable angina, or high-risk **coronary stenoses** were treated with heparin and aspirin and randomly assigned to additional treatment with placebo, a...

...treated with abciximab as a bolus and infusion had a significantly lower incidence of major **ischemic** complications or repeated revascularization than those given placebo. (Ref. 11) These favorable long-term effects were predominantly due to a reduced need for bypass surgery or repeated **angioplasty** , results consistent with a reduction in the incidence of clinical **restenosis** .|*Table 3.-Effectiveness of New Antithrombotic Approaches in **Coronary Angioplasty** *.**TABLE OMITTED...

...Indications for abciximab therapy during **coronary angioplasty** are evolving. Although large clinical studies such as EPIC and EPILOG prove that blockade of platelet glycoprotein IIb/IIIa receptors is useful during **angioplasty** , these studies do not define the details of optimal patient selection. The greatest treatment benefit...

...to anticoagulation with heparin, acute myocardial infarction, or postinfarction angina. Abciximab is also useful during **angioplasty** when unstable angina is associated with angiographic evidence of **thrombus** . Other indications, such as pretreatment for patients with unstable angina awaiting **coronary angioplasty** , are currently being evaluated in clinical trials...

...non-antibody-based blockers of platelet glycoprotein IIb/IIIa receptor have also been evaluated during **angioplasty** in multicenter, randomized clinical trials (Table 3). In the study entitled ``Integrelin to Minimize Platelet Aggregation and Prevent **Coronary Thrombosis** II,'' (Ref. 70) which involved 4010 patients undergoing **angioplasty** or atherectomy, high doses of the cyclic heptapeptide Integrilin were associated with a lower incidence of major **ischemic** complications or emergency revascularization than placebo at 24 hours (9.3 percent vs. 7.0...

...may relate to the irreversibility of action of abciximab or its cross-reactivity with other **vascular** receptors.

Thrombolytic Therapy as Adjunctive Therapy

Thrombolytic agents have been evaluated in clinical trials of PTCA. In the **Thrombolysis** and **Angioplasty** in Unstable Angina Trial, (Ref. 72) 469 patients with angina at rest who were ...receive placebo or intracoronary urokinase. Urokinase resulted in a lower incidence of angiographic evidence of **thrombus** during **angioplasty** (13.8 percent vs.

18.0 percent), but in higher rates of abrupt vessel closure...

...percent vs. 4.3 percent, P<0.02) and the combined end point of recurrent **ischemia** , myocardial infarction, or emergency bypass surgery (12.9 percent vs. 6.3 percent, P<0.02). (Ref. 72) In the **Thrombolysis** in Myocardial **Ischemia** (TIMI) IIIB study, (Ref. 73) 1473 patients with unstable angina or non-Q-wave myocardial...
...These two studies suggest that **thrombolytic** therapy should not be used routinely during **angioplasty** for unstable angina. The deleterious effects of **thrombolytic** therapy in this setting may be caused by the platelet-activating actions of **thrombolytic** agents. (Ref. 74...

...Comparison of **Angioplasty** with Other Therapies
Choosing among medical therapy, **angioplasty** , and surgical treatments remains a difficult decision in the care of individual patients with **coronary** **artery** disease. Nonetheless, the results of several clinical trials allow general guidelines to be developed.
PTCA...

...PTCA has been compared with medical therapy for stable angina in two studies. In the **Angioplasty** Compared with Medicine study, (Ref. 75) patients with stable angina and single-vessel **coronary** disease were randomly assigned to treatment with PTCA or medical therapy. In the Medicine, **Angioplasty** , or Surgery Study, (Ref. 76) patients with stable angina and a **stenosis** in the proximal left anterior descending **artery** were randomly assigned to medical therapy, PTCA, or bypass surgery with the left internal thoracic **artery** (Table 4). Both studies suggested that PTCA provides more complete relief of angina than medical...
...of myocardial infarction or bypass surgery (Table 4).|*Table 4.-Comparison of Medical Therapy and **Coronary** **Angioplasty** in Patients with Stable Angina, Unstable Angina, or Non-Q-Wave Myocardial Infarction *.**TABLE OMITTED...

...with unstable angina or non-Q-wave myocardial infarction. An aggressive strategy of early cardiac **catheterization** with **angioplasty** was compared with a conservative strategy of medical therapy for patients presenting with **ischemic** pain at rest (Table 4). Although major complications occurred with similar frequencies in patients assigned...

...infarction (Table 5). A meta-analysis of several reports suggested that PTCA performed without antecedent **thrombolytic** therapy results in a lower risk of death or reinfarction than **thrombolytic** therapy. (Ref. 78) Whether PTCA can be used successfully in a broad range of settings...

...the Myocardial Infarction Triage and Intervention Registry showed nearly identical hospital mortality rates for direct **angioplasty** and **thrombolytic** therapy for acute myocardial infarction in 19 Seattle hospitals (5.5 percent vs. 5.6 percent). (Ref. 79)|*Table 5.-Comparison of Medical Therapy and **Coronary** **Angioplasty** in Patients with Acute Myocardial Infarction (MI) *.**TABLE OMITTED...
...the results of clinical trials comparing PTCA with medical therapy suggest that the benefit of **angioplasty** depends on the severity and acuity of the clinical presentation. A gradient of risk extends across the spectrum of patients with **coronary** **artery** disease treated medically (Tables 4 and 5). At one end of the spectrum, patients with stable angina and mild **coronary** **artery** disease treated medically are at low risk of death or nonfatal myocardial infarction. In this...

...procedures. At the other end of the spectrum, patients with acute myocardial infarction treated with **thrombolytic** therapy have a risk of major complications such as reinfarction or stroke that may be reduced with early **angioplasty** . In the middle of the spectrum, patients with unstable angina treated medically have an intermediate risk of major **ischemic** complications. In this setting, PTCA provides symptomatic relief and stabilizes ...Several studies have compared PTCA with bypass surgery for patients with single-vessel or multivessel **coronary** **artery** disease. Despite the use of different protocols, these studies have yielded consistent results (Table 6). (Ref. 76,80-84) Major **ischemic**

complications, such as death or myocardial infarction, occur with similar frequencies one to five years after **angioplasty** or bypass surgery. The chief difference between the two strategies is the increased need for repeated revascularization procedures in patients who initially underwent PTCA. In the Bypass **Angioplasty** Revascularization Investigation (BARI), however, 69 percent of patients initially treated with **angioplasty** had not undergone bypass surgery five years later. (Ref. 81)|*Table 6.-Comparison of Surgical Therapy and **Coronary** **Angioplasty** *.**TABLE OMITTED...

...Thus, patients with single-vessel or multivessel **coronary** **artery** disease who are good candidates for either **angioplasty** or bypass surgery can be reassured that both revascularization approaches are followed by equivalent rates of major **ischemic** complications. However, diabetic patients had higher rates of **restenosis** than patients without diabetes (Ref. 85) and significantly higher rates of survival five years after treatment with bypass surgery than with **coronary** **angioplasty** in BARI (81 percent vs. 65 percent, P = 0.003). (Ref. 81) In the absence of other factors affecting surgical risk, the decision about surgical therapy or **angioplasty** can be based on personal preference, weighing the invasive nature of bypass surgery against the likelihood of repeated procedures after **angioplasty** .

Relation between Severity of **Stenosis** and Clinical Outcome

Why have **coronary** interventional therapies not improved the natural history of **coronary** **artery** disease more substantially? Although it seems intuitive that the risk of complications from **coronary** atherosclerosis should correlate with the angiographic severity of individual **coronary** - **artery** lesions, several studies have discounted this notion...

...of lesions and clinical events. In the Familial Atherosclerosis Treatment Study, (Ref. 86) men with **coronary** **artery** disease were randomly assigned to treatment with placebo or one of two lipid-lowering regimens...

...despite a slight 0.3 and 1.1 percentage-point reduction in the severity of **stenosis** in the two groups receiving active treatment. Myocardial infarction occurred in 19 percent of the...

...Although lipid-lowering therapy does not reduce the likelihood of **restenosis** six months after **coronary** **angioplasty** , (Ref. 87) it does reduce the likelihood of angina or myocardial infarction and the need...

...with hypercholesterolemia. Intensive lipid-lowering therapy was associated with a 34 percent reduction in major **ischemic** events and a 37 percent reduction in the rate of bypass surgery or PTCA in...

...Ref. 89) The mechanism for this benefit has been attributed to minor regression of fixed **stenoses** , generalized improvement in endothelial function, and a decreased risk of **plaque** rupture during lipid-lowering therapy. (Ref. 90,91...

...The dissociation between the severity of **stenosis** and the risk of major **ischemic** complications has been confirmed in several other settings. Ambrose and colleagues (Ref. 92) compared **coronary** **stenoses** in 38 patients who had myocardial infarction in the interval between two **coronary** **arteriographic** studies. The lesions seen on the initial angiogram that were later responsible for Q-wave myocardial infarctions had a mean **stenosis** of only 34 percent. In a similar study, Little and colleagues (Ref. 93) reviewed serial **coronary** **arteriograms** in 42 consecutive patients before and after acute myocardial infarction. In 29 patients, a new total **occlusion** was observed on the second **arteriogram** . Among these 29 patients, 66 percent of the culprit lesions were associated with **stenoses** of less than 50 percent on the initial **arteriogram** .

...

...Thus, the emphasis on the severity of **stenosis** wrongly reinforces the simplistic notion that angiographically severe lesions are associated with

an increased risk of death or myocardial infarction. Whereas **coronary angioplasty** is appropriate to reduce symptoms in patients with angina and angiographically severe lesions, because these are frequently associated with decreased **coronary** flow reserve and myocardial **ischemia** , (Ref. 94) this therapy cannot be expected to eliminate all subsequent cardiovascular risk, because **coronary** atherosclerosis is a diffuse process (Ref. 95) and angiographically mild **stenoses** not conventionally targeted for treatment are inherently more likely than severe lesions to cause myocardial...

...Although **coronary arteriography** provides a high-resolution image of the **coronary lumen** , it may not be ideal for evaluating the severity of **coronary** atherosclerosis -- a disease of the vessel wall. Additional information about **coronary** atherosclerosis may be obtained with new imaging techniques and physiologic measurements. **Intravascular** ultrasound imaging provides anatomical details of the vessel wall and atherosclerotic **plaque** that are helpful in some **coronary** interventions. (Ref. 96) Several studies are under way to determine whether ultrasound findings are associated...

...PTCA has been a major therapeutic advance because it relieves angina in patients with severe **stenoses** . **Coronary** stenting has revolutionized the practice of interventional cardiology by partially overcoming some of the limitations of **coronary angioplasty** , such as abrupt vessel closure and **restenosis** . Ongoing studies of stent coatings and optimal antithrombotic therapies may improve the success of **coronary** -stent implantation, further reduce the rate of **restenosis** , and lower the risk of death or nonfatal myocardial infarction...

...Platelet glycoprotein IIb/IIIa-receptor blockers have reduced the rate of acute complications of **coronary angioplasty** in high-risk settings and may have persistent benefits after discharge from the hospital. Further ...

...evaluate the role of these agents as treatment for unstable angina or myocardial infarction before **coronary angioplasty** is performed...

...In general, the treatment effect of mechanical **coronary** interventions is confined to discrete **coronary - artery** segments, whereas the pathologic process of **coronary** atherosclerosis is diffuse. **Coronary** interventional therapy should thus be viewed as part of a comprehensive strategy involving other treatments...

CITED REFERENCES

...Roubin GS, Schweiger M, et al. Length of hospital stay and complications after percutaneous transluminal **coronary angioplasty** : clinical and procedural predictors. Circulation 1995;92:311-9.

3. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of directional atherectomy with **coronary angioplasty** in patients with **coronary artery** disease. N Engl J Med 1993;329:221-7.
4. Adelman AG, Cohen EA, Kimball BP, et al. A comparison of directional atherectomy with **balloon angioplasty** for lesions of the left anterior descending **coronary artery** . N Engl J Med 1993;329:228-33.
5. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of **balloon** -expandable-stent implantation with **balloon angioplasty** in patients with **coronary artery** disease. N Engl J Med 1994;331:489-95.
6. Fischman DL, Leon MB, Baim DS, et al. A randomized comparison of **coronary** -stent placement and **balloon angioplasty** in the treatment of **coronary artery** disease. N Engl J Med 1994;331:496-501.
7. Ellis SG, Cowley MJ, Whitlow PL, et al. Prospective case-control comparison of percutaneous transluminal **coronary** revascularization in patients with multivessel disease treated in 1986-1987 versus 1991: improved in-hospital...

...1995;25:1137-42.

8. Detre K, Holubkov R, Kelsey S, et al. Percutaneous transluminal **coronary angioplasty** in 1985-1986 and 1977-1981: the National Heart, Lung, and Blood Institute Registry. N...

...J Med 1988;318:265-70.

9. Nobuyoshi M, Kimura T, Nosaka H, et al. **Restenosis** after successful percutaneous transluminal **coronary angioplasty** : serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616-23...

...of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk **coronary angioplasty** . N Engl J Med 1994;330:956-61.
11. Topol EJ, Califf RM, Weisman HF, et al. Randomised trial of **coronary** intervention with antibody against platelet IIb/IIIa integrin for reduction of clinical **restenosis** : results at six months. Lancet 1994;343:881-6.
12. Topol EJ. Evaluation of PTCA...

...Cardiology, Birmingham, England, August 27, 1996.
13. Landau C, Lange RA, Hillis LD. Percutaneous transluminal **coronary angioplasty** . N Engl J Med 1994;330:981-93.
14. Lemaitre DT, Barber AP, Mullen MG...

...1996:1-32.
15. Kuntz RE, Gibson CM, Nobuyoshi M, Baim DS. Generalized model of **restenosis** after conventional **balloon angioplasty** , stenting and directional atherectomy. J Am Coll Cardiol 1993;21:15-25.
16. Roubin GS, Douglas JS Jr, King SB III, et al. Influence of **balloon** size on initial success, acute complications, and **restenosis** after percutaneous transluminal **coronary angioplasty** : a prospective randomized study. Circulation 1988;78:557-65.
17. Holmes DR Jr, Topol EJ, Califf RM, et al. A multicenter, randomized trial of **coronary angioplasty** versus directional atherectomy for patients with saphenous **vein** bypass graft lesions: CAVEAT-II Investigators. Circulation 1995;91:1966-74.
18. Appelman YEA, Piek JJ, Strikwerda S, et al. Randomised trial of excimer laser **angioplasty** versus **balloon angioplasty** for treatment of **obstructive coronary artery** disease. Lancet 1996;347:79-84.
19. Appelman YEA, Koolen JJ, Piek JJ, et al. Excimer laser **angioplasty** versus **balloon angioplasty** in functional and total **coronary occlusions** . Am J Cardiol 1996;78:757-62.
20. Bittl JA. Directional **coronary** atherectomy versus **balloon angioplasty** . N Engl J Med 1993;329:273-4.
21. Harrington RA, Lincoff AM, Califf RM, et al. Characteristics and consequences of myocardial infarction after percutaneous **coronary** intervention: insights from the **Coronary Angioplasty** Versus Excisional Atherectomy Trial (CAVEAT). J Am Coll Cardiol 1995;25:1693-9.
22. Elliott JM, Berdan LG, Holmes DR, et al. One-year follow-up in the **Coronary Angioplasty** Versus Excisional Atherectomy Trial (CAVEAT I). Circulation 1995;91:2158-66.
23. Baim DS, Simonton CA, Popma JJ, et al. Mechanism of **lumen** enlargement by optimal a therectomy -- IVUS insights from the OARS Study. J Am Coll Cardiol...

...Suppl A:291A. abstract.
24. Mintz GS, Kovach JA, Javier SP, et al. Mechanisms of **lumen** enlargement after excimer laser **coronary angioplasty** : an **intravascular** ultrasound study. Circulation 1995;92:3408-14.
25. Baumbach A, Bittl JA, Fleck E, et al. Acute complications of excimer laser **coronary angioplasty** : a detailed analysis of multicenter results. J Am Coll Cardiol 1994;23:1305-13.
26. Bittl JA, Ryan TJ Jr, Keaney JF Jr, et al. **Coronary artery** perforation during excimer laser **coronary angioplasty** . J Am Coll Cardiol 1993;21:1158-65.
27. van Leeuwen TG, Meertens JH, Velema E, Post MJ, Borst C. Intraluminal vapor bubble induced by excimer laser pulse causes microsecond **arterial** dilation and invagination leading to extensive wall damage in the rabbit. Circulation 1993;87:1258...

...MK, Bittl JA, et al. Effect of intracoronary saline infusion on dissection during excimer laser **coronary angioplasty** : a randomized trial. J Am Coll Cardiol 1995;26:1264-9.

29. Safian RD, Niazi...

...Strzelecki M, et al. Detailed angiographic analysis of high-speed mechanical rotational atherectomy in human **coronary arteries** . Circulation 1993;88:961-8.
30. MacIsaac AI, Bass TA, Buchbinder M, et al. High speed rotational atherectomy: outcome in calcified and noncalcified **coronary artery** lesions. J Am Coll Cardiol 1995;26:731-6.
31. Vandormael M, Reifart N, Preusler W, et al. Six months follow-up results following excimer laser **angioplasty** , rotational atherectomy and **balloon angioplasty** for complex lesions: ERBAC Study. Circulation 1994;90:Suppl:I-213. abstract.
32. de Muinck ED, den Heijer P, van Dijk RB, et al. Autoperfusion **balloon** versus stent for acute or threatened closure during percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1994;74:1002-5.
33. Lincoff AM, Topol EJ, Chapekis AT, et al. Intracoronary stenting compared with conventional therapy for abrupt vessel closure complicating **coronary angioplasty** : a matched case-control study. J Am Coll Cardiol 1993;21:866-75.
34. Roubin...

...AD, Agrawal SK, et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal **coronary angioplasty** . Circulation 1992;85:916-27.
35. Lincoff AM, Popma JJ, Ellis SG, Hacker JA, Topol EJ. Abrupt vessel closure complicating **coronary angioplasty** : clinical, angiographic and therapeutic profile. J Am Coll Cardiol 1992;19:926-35.
36. White CJ, Ramee SR, Collins TJ, Jain SP, Escobar A. **Coronary** angioscopy of abrupt **occlusion** after **angioplasty** . J Am Coll Cardiol 1995;25:1681-4.
37. Sutton JM, Ellis SG, Roubin GS, et al. Major clinical events after **coronary** stenting: the multicenter registry of acute and elective Gianturco-Roubin stent placement. Circulation 1994;89...

...37.
38. Hasdai D, Garratt KN, Holmes DR Jr, Berger PB, Schwartz RS, Bell MR. **Coronary angioplasty** and intracoronary **thrombolytics** are of limited efficacy in resolving early intracoronary stent **thrombosis** . J Am Coll Cardiol 1996;28:361-7.
39. Macaya C, Serruys PW, Ruygrok P, et al. Continued benefit of **coronary** stenting versus **balloon angioplasty** : one-year clinical follow-up of Benestent trial. J Am Coll Cardiol 1996;27:255...

...T, Yokoi H, Nakagawa Y, et al. Three-year follow-up after implantation of metallic **coronary - artery** stents. N Engl J Med 1996;334:561-6.
41. Itoh A, Colombo A, Hall P, et al. Stenting in protected and unprotected left main **coronary artery** : immediate and follow-up results. J Am Coll Cardiol 1996;27:Suppl A:277A. abstract...

...Piana RN, Moscucci M, Cohen DJ, et al. Palmaz-Schatz stenting for treatment of focal **vein** graft **stenosis** : immediate results and long-term outcome. J Am Coll Cardiol 1994;23:1296-304.
43...

...DS, Schatz RS, et al. Immediate results and late outcomes after stent implantation in saphenous **vein** graft lesions: the multicenter U.S. Palmaz-Schatz stent experience. J Am Coll Cardiol 1995...
...SL, Colombo A, Maiello L, Borrione M, Finci L, Almagor Y. Intracoronary stent insertion after **balloon angioplasty** of chronic total **occlusions** . J Am Coll Cardiol 1995;26:713-9.
45. Serruys PW, Leon M, Hamburger JN, et al. Recanalization of chronic total **coronary occlusions** using a laser guide wire: the EU and US TOTAL experience. J Am Coll Cardiol...

...abstract.
46. Popma JJ, Coller BS, Ohman EM, et al. Antithrombotic therapy in patients undergoing **coronary angioplasty** . Chest 1995;108:Suppl:486S-501S.

47. Mak K-H, Belli G, Ellis SG, Moliterno DJ. Subacute stent **thrombosis** : evolving issues and current concepts. J Am Coll Cardiol 1996;27:494-503.
48. Bittl JA. Subacute stent **occlusion** : **thrombus** horribilis. J Am Coll Cardiol 1996;28:368-70.
49. Colombo A, Hall P, Nakamura S, et al. Intracoronary stenting without anticoagulation accomplished with **intravascular** ultrasound guidance. Circulation 1995;91:1676-88.
50. Neumann F-J, Gawaz M, Ott I, May A, Mossmer G, Schomig A. Prospective evaluation of hemostatic predictors of subacute stent **thrombosis** after **coronary** Palmaz-Schatz stenting. J Am Coll Cardiol 1996;27:15-21.
51. Schomig A, Neumann...

...A, et al. A randomized comparison of antiplatelet and anticoagulation therapy after the placement of **coronary - artery** stents. N Engl J Med 1996;334:1084-9.
52. Serruys PW, Emanuelsson H, van der Giessen W, et al. Heparin-coated Palmaz-Schatz stents in human **coronary arteries** : early outcome of the Benestent-II Pilot Study. Circulation 1996;93:412-22.
53. Rogers C, Edelman ER. Endovascular stent design dictates experimental **restenosis** and **thrombosis** . Circulation 1995;91:2995-3001.
54. Currier JW, Faxon DP. **Restenosis** after percutaneous transluminal **coronary angioplasty** : have we been aiming at the wrong target? J Am Coll Cardiol 1995;25:516-20.
55. O'Brien ER, Alpers CE, Stewart DK, et al. Proliferation in primary and **restenotic coronary** atherectomy tissue: implications for antiproliferative therapy. Circ Res 1993;73:223-31.
56. Mintz GS, Popma JJ, Pichard AD, et al. **Intravascular** ultrasound predictors of **restenosis** after percutaneous transcatheter **coronary** revascularization. J Am Coll Cardiol 1996;27:1678-87.
57. Mintz GS, Popma JJ, Pichard AD, et al. **Arterial** remodeling after **coronary angioplasty** : a serial **intravascular** ultrasound study. Circulation 1996;94:35-43.
58. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of human atherosclerotic **coronary arteries** . N Engl J Med 1987;316:1371-5.
59. Kakuta T, Currier JW, Haudenschild **CC** , Ryan TJ, Faxon DP. Differences in compensatory vessel enlargement, not intimal formation, account for **restenosis** after **angioplasty** in the hypercholesterolemic rabbit model. Circulation 1994;89:2809-15.
60. Strauss BH, Chisholm RJ, Keeley FW, Gotlieb AI, Logan RA, Armstrong PW. Extracellular matrix remodeling after **balloon angioplasty** injury in a rabbit model of **restenosis** . Circ Res 1994;75:650-8.
61. Dussaillant GR, Mintz GS, Pichard AD, et al. Small stent size and intimal hyperplasia contribute to **restenosis** : a volumetric **intravascular** ultrasound analysis. J Am Coll Cardiol 1995;26:720-4.
62. Fernandez-Ortiz A, Badimon JJ, Falk E, et al. Characterization of the relative **thrombogenicity** of atherosclerotic **plaque** components: implications for consequences of **plaque** rupture. J Am Coll Cardiol 1994;23:1562-9.
63. Merino A, Cohen M, Badimon JJ, Fuster V, Badimon L. Synergistic action of severe wall injury and shear forces on **thrombus** formation in **arterial stenosis** : definition of a **thrombotic** shear rate threshold. J Am Coll Cardiol 1994;24:1091-7.
64. Marmur JD, Merlini PA, Sharma SK, et al. **Thrombin** generation in human **coronary arteries** after percutaneous transluminal **balloon angioplasty** . J Am Coll Cardiol 1994;24:1484-91.
65. Coughlin SR, Vu TK, Hung DT, Wheaton VI. Characterization of a functional **thrombin** receptor: issues and opportunities. J Clin Invest 1992;89:351-5.
66. Hirsh J, FusterA comparison of hirudin with heparin in the prevention of **restenosis** after **coronary angioplasty** . N Engl J Med 1995;333:757-63.
68. Bittl JA, Strony J, Brinker JA, et al. Treatment with bivalirudin (Hirulog) as compared with heparin during **coronary angioplasty** for unstable or postinfarction angina. N Engl J Med 1995;333:764-9.
69. Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of

coronary artery disease and the acute **coronary** syndromes. N Engl J Med 1992;326:242-50, 310-8.
70. Tcheng JE, Lincoff...

...Sigmon KN, Califf RM, Topol EJ. Platelet glycoprotein IIb/IIIa inhibition with Integrelin during percutaneous **coronary** intervention: the IMPACT II Trial. Circulation 1995;92:Suppl I:I-543. abstract.
71. Horrigan...
...27:Suppl A:55A. abstract.
72. Ambrose JA, Almeida OD, Sharma SK, et al. Adjunctive **thrombolytic** therapy during **angioplasty** for **ischemic** rest angina: results of the TAUSA Trial. Circulation 1994;90:69-77.
73. The TIMI...

...1994;89:1545-56.
74. Eisenberg PR, Sobel BE, Jaffe AS. Activation of prothrombin accompanying **thrombolysis** with recombinant tissue-type plasminogen activator. J Am Coll Cardiol 1992;19:1065-9.
75. Parisi AF, Folland ED, Hartigan P. A comparison of **angioplasty** with medical therapy in the treatment of single-vessel **coronary artery** disease. N Engl J Med 1992;326:10-6.
76. Hueb WA, Bellotti G, de Oliveira SA, et al. The Medicine, **Angioplasty** , or Surgery Study (MASS): a prospective, randomized trial of medical therapy, **balloon angioplasty** or bypass surgery for single proximal left anterior descending **artery stenoses** . J Am Coll Cardiol 1995;26:1600-5.
77. Anderson HV, Cannon CP, Stone PH, et al. One-year results of the **Thrombolysis** in Myocardial Infarction (TIMI) IIIB clinical trial: a randomized comparison of tissue-type plasminogen activator...
...85.
79. Every NR, Parsons LS, Hlatky M, Martin JS, Weaver WD. A comparison of **thrombolytic** therapy with primary **coronary angioplasty** for acute myocardial infarction. N Engl J Med 1996;335:1253-60.
80. Pocock SJ, Henderson RA, Rickards AF, et al. Meta-analysis of randomised trials comparing **coronary angioplasty** with bypass surgery. Lancet 1995;346:1184-9.
81. The Bypass **Angioplasty** Revascularization Investigation (BARI) Investigators. Comparison of **coronary** bypass surgery with **angioplasty** in patients with multivessel disease. N Engl J Med 1996;335:217-25.
82. Hamm...

...Reimers J, Ischinger T, Rupprecht H-J, Berger J, Bleifield W. A randomized study of **coronary angioplasty** compared with bypass surgery in patients with symptomatic multivessel **coronary** disease. N Engl J Med 1994;331:1037-43.
83. King SB III, Lembo NJ, Weintraub WS, et al. A randomized trial comparing **coronary angioplasty** with **coronary** bypass surgery. N Engl J Med 1994;331:1044-50.
84. RITA Trial Participants. **Coronary angioplasty** versus **coronary artery** bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. Lancet 1993;341:573-80.
85. Aronson D, Bloomgarden Z, Rayfield EJ. Potential mechanisms promoting **restenosis** in diabetic patients. J Am Coll Cardiol 1996;27:528-35.
86. Brown G, Albers JJ, Fisher LD, et al. Regression of **coronary artery** disease as a result of intensive lipid-lowering therapy in men with high levels of...

...87. Weintraub WS, Boccuzzi SJ, Klein JL, et al. Lack of effect of lovastatin on **restenosis** after **coronary angioplasty** . N Engl J Med 1994;331:1331-7.
88. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with **coronary** heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383-9.
89. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on **coronary** events after myocardial infarction in patients with average cholesterol levels. N Engl J Med 1996...

...CB, Klein JL, Weintraub WS, et al. Beneficial effects of cholesterol-lowering therapy on the **coronary** endothelium in patients with **coronary** **artery** disease. N Engl J Med 1995;332:481-7.
91. Anderson TJ, Meredith IT, Yeung...
...Selwyn AP, Ganz P. The effect of cholesterol-lowering and antioxidant therapy on endothelium-dependent **coronary** vasomotion. N Engl J Med 1995;332:488-93.
92. Ambrose JA, Tannenbaum MA, Alexopoulos D, et al. Angiographic progression of **coronary** **artery** disease and the development of myocardial infarction. J Am Coll Cardiol 1988;12:56-62.
93. Little WC, Constantinescu M, Applegate RJ, et al. Can **coronary** angiography predict the site of a subsequent myocardial infarction in patients with mild-to-moderate **coronary** **artery** disease? Circulation 1988;78:1157-66.
94. Uren NG, Melin JA, De Bruyne B, Wijns W, Baudhuin T, Camici PG. Relation between myocardial blood flow and the severity of **coronary** - **artery** **stenosis** . N Engl J Med 1994;330:1782-8.
95. Mintz GS, Painter JA, Pichard AD, et al. Atherosclerosis in angiographically ``normal'' **coronary** **artery** reference segments: an **intravascular** ultrasound study with clinical correlations. J Am Coll Cardiol 1995;25:1479-85.
96. Topol EJ, Nissen SE. Our preoccupation with **coronary** luminology: the dissociation between clinical and angiographic findings in **ischemic** heart disease. Circulation 1995;92:2333-42.
97. The GUIDE Trial Investigators. IVUS-determined predictors of **restenosis** in PTCA and DCA: final report from the GUIDE Trial, Phase II. J Am Coll...

39/5,K/52 (Item 7 from file: 444)

00114920

A Comparison of Hirudin with Heparin in the Prevention of Restenosis **after** Coronary Angioplasty **(Original Articles)**

Serruys, Patrick W.; Herrman, Jean-Paul R.; Simon, Rudiger; Rutsch, Wolfgang; Bode, Christoph; Laarman, Gert-Jan; van Dijk, Rene; van den Bos, Arjan A.; Umans, Victor A.W.M.; Fox, Keith A.A.; Close, Philip; Deckers, Jaap W.; the Helvetica Investigators.
The New England Journal of Medicine
Sep 21, **1995** ; 333 (12),pp 757-763
LINE COUNT: 00454 WORD COUNT: 06277
ISSN: 0028-4793
CORPORATE SOURCE: From the Academisch Ziekenhuis Dijkzigt, Rotterdam, the Netherlands (P.W.S., J.-P.R.H., V.A.W.M.U.); the Medizinische Universitatsklinik, Kiel, Germany (R.S.); the Universitatsklinik Rudolf Virchow, Berlin, Germany (W.R.); the Medizinische Klinik III, Heidelberg, Germany (C.B.); the Onze Lieve Vrouwe Gasthuis, Amsterdam (G.-J.L.); the Academisch Ziekenhuis Groningen, Groningen, the Netherlands (R.D.); the Medisch Centrum de Klokkenberg, Breda, the Netherlands (A.A.B.); the Royal Infirmary, Edinburgh, United Kingdom (K.A.A.F.); Ciba-Geigy Ltd., Basel, Switzerland (P.C.); and Cardialysis B.V., Rotterdam, the Netherlands (J.W.D.). Address reprint requests to Dr. Serruys at the Thoraxcenter, Erasmus University, Rm. EE 2332, P.O. Box 1738, 3000 DR Rotterdam, the Netherlands.----------| *: The institutions and investigators participating in the Helvetica trial are listed in the Appendix.

Abstract

Background: The likelihood of **restenosis** is a major limitation of **coronary** **angioplasty** . We studied whether hirudin, a highly selective inhibitor of **thrombin** with irreversible effects, would prevent **restenosis** after **angioplasty** . We compared two regimens of recombinant

hirudin with heparin.

Methods: We randomly assigned 1141 patients with unstable angina who were scheduled for **angioplasty** to receive one of three treatments: (1) a bolus dose of 10,000 IU of heparin followed by an **intravenous** infusion of heparin for 24 hours and subcutaneous placebo twice daily for three days (382 patients), (2) a bolus dose of 40 mg of hirudin followed by an **intravenous** infusion of hirudin for 24 hours and subcutaneous placebo twice daily for three days (381 patients), or (3) the same hirudin regimen except that 40 mg of hirudin was given subcutaneously instead of placebo twice daily for three days (378 patients). The primary end point was event-free survival at seven months. Other end points were early cardiac events (within 96 hours), bleeding and other complications of the study treatment, and angiographic measurements of **coronary** diameter at six months of follow-up.

Results: At seven months, event-free survival was 67.3 percent in the group receiving heparin, 63.5 percent in the group receiving **intravenous** hirudin, and 68.0 percent in the group receiving both **intravenous** and subcutaneous hirudin (P = 0.61). However, the administration of hirudin was associated with a significant reduction in early cardiac events, which occurred in 11.0, 7.9, and 5.6 percent of patients in the respective groups (combined relative risk with hirudin, 0.61; 95 percent confidence interval, 0.41 to 0.90; P = 0.023). The mean minimal luminal diameters in the respective groups on follow-up angiography at six months were 1.54, 1.47, and 1.56 mm (P = 0.08).

Conclusions: Although significantly fewer early cardiac events occurred with hirudin than with heparin, hirudin had no apparent benefit with longer-term follow-up. (N Engl J Med 1995;333:757-63.)

CITED REFERENCES

1. Stein B, Fuster V, Israel DH, et al. Platelet inhibitor agents in cardiovascular disease: an update. J Am Coll Cardiol 1989;14:813-36.
2. Coller BS. Platelets and **thrombolytic** therapy. N Engl J Med 1990;322:33-42.
3. Chesebro JH, Webster MWI, Zoldhelyi P, Roche PC, Badimon L, Badimon JJ. Antithrombotic therapy and progression of **coronary artery** disease: antiplatelet versus antithrombins. Circulation 1992;86:Suppl III:III-100-III-110.
4. Schwartz RS, Murphy JG, Edwards WD, Camrud AR, Vlietstra RE, Holmes DR. **Restenosis** after **balloon angioplasty** : a practical proliferative model in porcine **coronary arteries** . Circulation 1990;82:2190-200.
5. McNamara CA, Sarembock IJ, Gimple LW, Fenton JW II, Coughlin SR, Owens GK. **Thrombin** stimulation of smooth muscle cell proliferation is mediated by a cleavage-dependent, receptor mechanism. In: Abstracts of the Fourth **Restenosis** Summit, Cleveland, May 28-29, 1992. Cleveland: Cleveland Clinic Foundation, 1992:18. abstract.
6. Grutter MG, Priestle JP, Rahuel J, et al. Crystal structure of the **thrombin** -hirudin complex: a novel mode of serine protease inhibition. EMBO J 1990;8:2361-5.
7. Weitz JI, Hudoba M, Massel D, Maraganore J, Hirsh J. Clot-bound **thrombin** is protected from inhibition by heparin-antithrombin III but is susceptible to inactivation by antithrombin III-independent inhibitors. J Clin Invest 1990;86:385-91.
8. Heras M, Chesebro JH, Webster MWI, et al. Hirudin, heparin, and placebo during deep **arterial** injury in the pig: the in vivo role of **thrombin** in platelet-mediated **thrombosis** . Circulation 1990;82:1476-84.
9. Sarembock IJ, Gertz SD, Gimple LW, Owen RM, Powers ER, Roberts WC. Effectiveness of recombinant desulphatohirudin in reducing **restenosis** after **balloon angioplasty** of atherosclerotic femoral **arteries** in rabbits. Circulation 1991;84:232-43.
10. Goldman L, Hashimoto B, Cook EF, Loscalzo A. Comparative reproducibility and validity of systems for assessing cardiovascular functional class: advantages of a new specific activity scale. Circulation 1981;64:1227-34.
11. Braunwald E. Unstable angina: a classification. Circulation 1989;80:410-4.
12. Close P, Bichler J, Kerry R, et al. Weak allergenicity of recombinant hirudin CGP 39393 (REVASC) in immunocompetent volunteers. Coron **Artery** Dis 1994;5:943-9.

13. Blackburn H, Keys A, Simonson E, Rautaharju P, Punsar S. The electrocardiogram in population studies: a classification system. Circulation 1960;21:1160-75.
14. Hull R, Hirsch J, Jay R, et al. Different intensities of oral anticoagulant therapy in the treatment of proximal- **vein thrombosis** . N Engl J Med 1982;307:1676-81.
15. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of **balloon** -expandable stent implantation with **balloon angioplasty** in patients with **coronary artery** disease. N Engl J Med 1994;331:489-95.
16. Serruys PW, Foley DP, de Feyter PJ, eds. Quantitative **coronary** angiography in clinical practice. Dordrecht, the Netherlands: Kluwer Academic Publishers, 1994.
17. Kalbfleisch JD, Prentice RL. The statistical analysis of failure time data. New York: John Wiley, 1980.
18. Schwartz L, Bourassa MG, Lesperance J, et al. Aspirin and dipyridamole in the prevention of **restenosis** after percutaneous transluminal **coronary angioplasty** . N Engl J Med 1988;318:1714-9.
19. Chesebro JH, Webster MWI, Reeder GS, et al. **Coronary angioplasty** : antiplatelet therapy reduces acute complications but not **restenosis** . Circulation 1989;80:Suppl II:II-64. abstract.
20. Bertrand ME, Allain H, Lablanche JM. Results of a randomized trial of ticlopidine versus placebo for prevention of acute closure and **restenosis** after **coronary angioplasty** (PTCA): the TACT study. Circulation 1990;82:Suppl III:III-190. abstract.
21. Topol EJ, Califf RM, Weisman HF, et al. Randomised trial of **coronary** intervention with antibody against platelet IIb/IIIa integrin for reduction of clinical **restenosis** : results at six months. Lancet 1994;343:881-6.
22. The EPIC Investigators. Use of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk **coronary angioplasty** . N Engl J Med 1994;330:956-61.
23. Verstraete M, Nurmohamed M, Kienast J, et al. Biologic effects of recombinant hirudin (CGP 39393) in human volunteers. J Am Coll Cardiol 1993;22:1080-8.
24. Eriksson BI, Kalebo P, Ekman S, Lindbratt S, Kerry R, Close P. Direct **thrombin** inhibition with rec-hirudin CGP 39393 as prophylaxis of **thromboembolic** complications after total hip replacement. **Thromb** Haemost 1994;72:227-31.
25. van den Bos AA, Deckers JW, Heyndrickx GR, et al. Safety and efficacy of recombinant hirudin (CGP 39 393) versus heparin in patients with stable angina undergoing **coronary angioplasty** . Circulation 1993;88:2058-66.
26. Zoldhelyi P, Bichler J, Owen WG, et al. Persistent **thrombin** generation in humans during specific **thrombin** inhibition with hirudin. Circulation 1994;90:2671-8.
27. Chesebro JH, Badimon L, Fuster V. Importance of antithrombin therapy during **coronary angioplasty** . J Am Coll Cardiol 1991;17:Suppl B:96B-100B.
28. Wilentz JR, Sanborn TA, Haudenschild **CC** , Valeri CR, Ryan TJ, Faxon DP. Platelet accumulation in experimental **angioplasty** : time course and relation to **vascular** injury. Circulation 1987;75:636-42.
29. Groves HM, Kinlough-Rathbone RL, Mustard JF. Development of nonthrombogenicity of injured rabbit aortas despite inhibition of platelet adherence. **Arteriosclerosis** 1986;6:189-95.
30. Steele PM, Chesebro JH, Stanson AW, et al. **Balloon angioplasty** : natural history of the pathophysiological response to injury in a pig model. Circ Res 1985;57:105-12.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

A Comparison of Hirudin with Heparin in the Prevention of Restenosis **after** Coronary Angioplasty **(Original Articles)**
1995 ;

Abstract

Background: The likelihood of **restenosis** is a major limitation of **coronary angioplasty** . We studied whether hirudin, a highly selective inhibitor of **thrombin** with irreversible effects, would prevent **restenosis** after **angioplasty** . We compared two regimens of recombinant

hirudin with heparin.

Methods: We randomly assigned 1141 patients with unstable angina who were scheduled for **angioplasty** to receive one of three treatments: (1) a bolus dose of 10,000 IU of heparin followed by an **intravenous** infusion of heparin for 24 hours and subcutaneous placebo twice daily for three days (382 patients), (2) a bolus dose of 40 mg of hirudin followed by an **intravenous** infusion of hirudin for 24 hours and subcutaneous placebo twice daily for three days (381...

...within 96 hours), bleeding and other complications of the study treatment, and angiographic measurements of **coronary** diameter at six months of follow-up.

Results: At seven months, event-free survival was 67.3 percent in the group receiving heparin, 63.5 percent in the group receiving **intravenous** hirudin, and 68.0 percent in the group receiving both **intravenous** and subcutaneous hirudin (P = 0.61). However, the administration of hirudin was associated with a...

TEXT

...Platelet aggregation, the generation of **thrombin** , and the release of growth factors at the site of **angioplasty** have all been implicated in the process of **restenosis** . (Ref. 1,2) Consequently, anticoagulants, antiplatelet agents, and specific antithrombin agents have been considered for the prevention of **restenosis** . (Ref. 3) **Thrombin** is the most potent platelet activator known, stimulating the production of platelet-derived growth factor and the secretion of prostacyclin, platelet-activating factor, and plasminogen-activator inhibitor. **Thrombin** has apparent mitogenic effects on lymphocytes and **vascular** smooth-muscle cells. (Ref. 4,5...

...compound originally extracted from the salivary gland of the leech, is a specific inhibitor of **thrombin** . The advantage of hirudin over other serine protease inhibitors is its potency in irreversibly blocking **thrombin** at multiple sites without the need for circulating antithrombin III. (Ref. 6) Because of the small size of the hirudin molecule, this substance can inhibit clot-bound **thrombin** and restrict the further formation of **thrombus** . (Ref. 7...

...Hirudin has reduced the deposition of platelets after **vascular** injury in pigs (Ref. 8) and lowered the rate of **restenosis** in hypercholesterolemic rabbits, (Ref. 9) providing a rationale for its use in patients undergoing **angioplasty** . In this trial we evaluated whether the inhibition of **thrombin** with hirudin as compared with heparin improved event-free survival in patients undergoing **coronary** **angioplasty** .

...

...Methods

Study Population

Patients with unstable angina and one or more clinically important new or **restenotic** **coronary** narrowings suitable for treatment with percutaneous transluminal **coronary** **angioplasty** were eligible for the study. From September 1992 through May 1993, 1154 patients from various...

...Ref. 11) The criteria for exclusion from the study were stable angina, a planned multistage **angioplasty** procedure or stent implantation, myocardial infarction occurring within the preceding two weeks, hypertension, diabetic retinopathy...

...The patients received one of the following three treatments: heparin (an **intravenous** bolus injection of 10,000 IU of heparin followed by a continuous **intravenous** infusion of 15 IU of heparin per kilogram of body weight per hour for 24 hours, with placebo given subcutaneously twice daily for three consecutive days), **intravenous** hirudin (an **intravenous** bolus injection of 40 mg of hirudin followed by a continuous **intravenous** infusion of 0.2 mg of hirudin per kilogram per hour for 24 hours, with placebo given subcutaneously twice daily for three consecutive days), or **intravenous** and subcutaneous hirudin (an **intravenous** bolus injection of 40 mg of hirudin followed by a continuous **intravenous** infusion of 0.2 mg

of hirudin per kilogram per hour for 24 hours, with 40 mg of hirudin given subcutaneously twice daily for three consecutive days). If the **angioplasty** lasted more than one hour, an additional bolus dose of 5000 IU of heparin could day of **angioplasty** , and this treatment was continued for at least 14 days.

Criteria for Evaluation

Efficacy

The primary end point was event-free survival 30 weeks after **angioplasty** -- that is, the absence of death, nonfatal myocardial infarction, **coronary - artery** bypass grafting or the use of a ``bailout'' procedure (e.g., stenting), or second **angioplasty** at previously dilated sites. Myocardial infarction was diagnosed on the basis of new Q waves...

...concomitant increase in the MB fraction. If a stent was implanted electively after the initial **angioplasty** (i.e., not as part of a bailout procedure), the implantation was considered equivalent to a second **angioplasty** . Second **angioplasty** or bypass surgery needed to be preceded by typical anginal symptoms or, if there were atypical anginal symptoms, by electrocardiographic evidence of myocardial **ischemia** at rest or during exercise and an angiographically determined **stenosis** greater than 50 percent by visual inspection...

...a ranked series of clinical events that included death from cardiac causes, nonfatal myocardial infarction, **coronary - artery** bypass grafting (or the use of a bailout procedure), second **angioplasty** , and anginal status (according to the classification system of the Canadian Cardiovascular Society (Ref. 10...

...the study medication; the minimal luminal diameter of the dilated sites as measured by quantitative **coronary** angiography at the 26-week follow-up evaluation; and any change in the minimal luminal diameter of dilated sites from immediately after **angioplasty** to follow-up angiography at 26 weeks ...

...bleeding that did not meet these criteria.

Angiography and Assessment of Coagulation

For each patient, **coronary** angiograms were obtained in a standardized fashion immediately before and immediately after **angioplasty** , and at the six-month follow-up evaluation. The angiograms were analyzed in a core...

...Blood samples for the measurement of coagulation were obtained at regular intervals before and after **angioplasty** . Blood samples for the determination of activated partial- **thromboplastin** times and levels of prothrombin fragment F(sub 1+2) (a measure of the generation of **thrombin**) were obtained separately by atraumatic venipuncture and were analyzed in a central laboratory.

Statistical Analysis...

...were compared in an intention-to-treat analysis, which included all randomized patients in whom **coronary angioplasty** was attempted. Patients in whom no **angioplasty** was attempted (i.e., those whose indication for **angioplasty** changed or disappeared) were excluded from the analysis. A successful procedure was defined as one in which the **stenosis** was reduced by more than half; in the case of a failed recanalization of a total **occlusion** , the second lesion treated was considered to be the first site of **angioplasty** .

...

...The minimal luminal diameters at the dilated sites 26 weeks after **angioplasty** were compared by analysis of variance, with the mean value for all sites used in cases of **angioplasty** at multiple sites. All reported P values are two-tailed. Whenever possible, estimates of the...of reasons. Thirteen patients were not included in the intention-to-treat analysis because no **angioplasty** was attempted. Among the remaining 1141 patients in whom **angioplasty** was attempted, 382 were randomly assigned to heparin, 381 to **intravenous** hirudin, and 378 to **intravenous** and subcutaneous hirudin. **Angioplasty** was successful in 91.7 percent, and the results of angiographic follow-up were available...

...The characteristics of the three groups were similar. Almost one third of the patients received **intravenous** heparin before randomization because of the severity of their unstable angina.|*Table 1.-Base-Line...

...TABLE OMITTED**

Efficacy

Among the study patients, 125 patients assigned to heparin, 139 assigned to **intravenous** hirudin, and 121 assigned to **intravenous** and subcutaneous hirudin reached a primary end point. The distribution of patients free of events...

...The incidence of early events (those occurring in the first 96 hours after **angioplasty**) is also shown in Table 2. Forty-two patients assigned to heparin, 30 patients assigned to **intravenous** hirudin, and 21 patients assigned to **intravenous** and subcutaneous hirudin had such events (relative risk in the combined hirudin groups, 0.61...

...6 percent in the heparin group, as compared with 5.3 percent among patients receiving **intravenous** hirudin and 12.3 percent among patients receiving **intravenous** and subcutaneous hirudin (combined relative risk with hirudin, 0.41; 95 percent confidence interval, 0...

...three myocardial infarctions and one nonhemorrhagic cerebrovascular accident resulted in death. In the group receiving **intravenous** hirudin, there was one sudden death. In the group receiving **intravenous** and subcutaneous hirudin, five patients had fatal myocardial infarctions. In this group there were alsoBase-line angiographic measurements and gains in luminal diameter achieved by **angioplasty** were similar in the three groups (Table 3). The changes in minimal luminal diameter from immediately after **angioplasty** to follow-up were also similar (Fig. 2).|*Table 3.-Mean (+/- SD) Angiographic Measurements in...

...OMITTED**|*FIGURE 2.-Cumulative Distribution of the Reduction in Minimal Luminal Diameter from Immediately after **Angioplasty** to Follow-up at Seven Months *.**FIGURE OMITTED**

Safety

The incidence of bleeding complications is...

...or minor bleeding were observed among groups. There were three cerebrovascular accidents. One patient receiving **intravenous** and subcutaneous hirudin was readmitted to the hospital with hemiplegia 14 hours after the final...

...condition, the patient died six days after the start of the study treatment. Two intracerebral **thrombotic** events were observed. One patient (receiving **intravenous** and subcutaneous hirudin), who presented with symptoms of neurologic deficit one day after discharge from...

...at the time of screening to 1.4 nmol per liter in the group receiving **intravenous** hirudin, and from 1.0 to 1.3 nmol per liter in the group receiving **intravenous** and subcutaneous hirudin), whereas in the heparin group the levels were slightly reduced (to 0...

...three groups.|*Figure 3.-Levels of Prothrombin Fragment F(sub 1+2) and Activated Partial- **Thromboplastin** Times in the Three Study Groups at Various Times before and after **Angioplasty** . A denotes the group receiving heparin, B the group receiving **intravenous** hirudin, and C the group receiving **intravenous** and subcutaneous hirudin. The solid area inside each box indicates the median value, and the...

...sub 1+2) (1.4 nmol per liter). Heparin tended to control the generation of **thrombin** better than hirudin both immediately after **angioplasty** and six hours after the start of the infusion. In the right-hand panel, the activated partial- **thromboplastin** time was measured up to a maximum of 150 seconds. Over the first 24 hours...

...Measurements of activated partial- **thromboplastin** time (Fig. 3) were higher at the end of the procedure in the subjects receiving...

...hours. The infusion of hirudin resulted in a more stable effect. Slightly prolonged activated partial- **thromboplastin** times were observed at 96 hours after **angioplasty** in the group receiving **intravenous** and subcutaneous hirudin...

...impressive reductions in the rate of major cardiac events in the first 96 hours after **angioplasty** as compared with heparin, the primary goal of this trial, a reduction in the rate...
...other trials using specific antiplatelet drugs have demonstrated beneficial effects on the acute complications of **coronary angioplasty** without favorably influencing long-term clinical outcomes. (Ref. 18-20) These findings differ from the results of the Evaluation of 7E3 for the Prevention of **Ischemic** Complications (EPIC) trial, (Ref. 21,22) in which the glycoprotein IIb/IIIa receptor was presumed...Primarily, the dosage was based on safety data obtained in healthy volunteers, stable patients undergoing **angioplasty** , and patients undergoing orthopedic surgery. (Ref. 23-25) However, the results of assays of prothrombin fragment F(sub 1+2) immediately after **angioplasty** suggest that the generation of **thrombin** was not satisfactorily inhibited in either hirudin group, whereas the dosage of heparin we used...

...at six hours. It can be inferred from these data that the adjustment in the **infusion rate** -- from 0.16 mg per kilogram per hour in the pilot study of patients with...

...hour in the current trial of patients with unstable angina and presumably higher levels of **thrombin** generation -- was too cautious a change in dosage. Zoldhelyi et al. (Ref. 26) recently reported failing to block the generation of **thrombin** in their patients despite the presence of a 10,000-fold molar excess of free hirudin over the amount bound in complexes with **thrombin** . **Infusion rates** of hirudin in experiments with animals were as much as five times higher than those...

...volunteers at a dose of 0.5 mg per kilogram twice daily, the activated partial- **thromboplastin** time 12 hours after the first injection was subtherapeutic, (Ref. 23) and it may be...

...paradox by which the early outcome is improved although there is less appropriate control of **thrombin** may be that the dosage used was not sufficient to produce an adequate level of anticoagulation, but was sufficient to limit the **thrombin** -mediated aggregation and activation of platelets, causing effects similar to those observed over the short...

...of treatment is unknown, even in animal models. Conflicting findings about the time course of **thrombogenicity** in the injured vessel wall have been reported. (Ref. 27-30) In this study we...

...the duration of hirudin administration and logistic considerations of the trial was presumably achieved by **administering** the **drug intravenously** for 24 hours and subcutaneously for three consecutive days ...
...A clearly beneficial effect of hirudin on platelet aggregation and **thrombus** formation was indicated by the prevention of acute **ischemic** events early after **angioplasty** . The failure of hirudin in this trial to alter longer-term outcomes indicates either that **thrombin** generation and **thrombus** formation in the period immediately after **angioplasty** may be less important in the process of **restenosis** than was previously believed or that complete reversal of the **thrombogenicity** of the injured vessel wall was not achieved or requires more time. Whether the large...

...participated in the Helvetica (Hirudin in a European Trial versus Heparin in the Prevention of **Restenosis** after PTCA) trial. The number of patients enrolled at each center is given in parentheses, followed by an asterisk when all patients in the cardiac **catheterization** laboratory at a center were screened and the results entered in a logbook...of Clinical Epidemiology and Biostatistics, Cardialysis -- R. Melkert. Hemostasis Core Laboratory (Department of Hemostasis and **Thrombosis** , Academic Medical

Center, Amsterdam) -- H. Buller. Safety Committee: K. Fox (chairman), H. Buller, D. Chamberlain...

CITED REFERENCES

...an update. J Am Coll Cardiol 1989;14:813-36.
2. Coller BS. Platelets and **thrombolytic** therapy. N Engl J Med 1990;322:33-42.
3. Chesebro JH, Webster MWI, Zoldhelyi P, Roche PC, Badimon L, Badimon JJ. Antithrombotic therapy and progression of **coronary artery** disease: antiplatelet versus antithrombins. Circulation 1992;86:Suppl III:III-100-III-110.
4. Schwartz RS, Murphy JG, Edwards WD, Camrud AR, Vlietstra RE, Holmes DR. **Restenosis** after **balloon angioplasty** : a practical proliferative model in porcine **coronary arteries** . Circulation 1990;82:2190-200.
5. McNamara CA, Sarembock IJ, Gimple LW, Fenton JW II, Coughlin SR, Owens GK. **Thrombin** stimulation of smooth muscle cell proliferation is mediated by a cleavage-dependent, receptor mechanism. In: Abstracts of the Fourth **Restenosis** Summit, Cleveland, May 28-29, 1992. Cleveland: Cleveland Clinic Foundation, 1992:18. abstract.
6. Grutter MG, Priestle JP, Rahuel J, et al. Crystal structure of the **thrombin** -hirudin complex: a novel mode of serine protease inhibition. EMBO J 1990;8:2361-5.
7. Weitz JI, Hudoba M, Massel D, Maraganore J, Hirsh J. Clot-bound **thrombin** is protected from inhibition by heparin-antithrombin III but is susceptible to inactivation by antithrombin...

...8. Heras M, Chesebro JH, Webster MWI, et al. Hirudin, heparin, and placebo during deep **arterial** injury in the pig: the in vivo role of **thrombin** in platelet-mediated **thrombosis** . Circulation 1990;82:1476-84.
9. Sarembock IJ, Gertz SD, Gimple LW, Owen RM, Powers ER, Roberts WC. Effectiveness of recombinant desulphatohirudin in reducing **restenosis** after **balloon angioplasty** of atherosclerotic femoral **arteries** in rabbits. Circulation 1991;84:232-43.
10. Goldman L, Hashimoto B, Cook EF, Loscalzo...

...R, et al. Weak allergenicity of recombinant hirudin CGP 39393 (REVASC) in immunocompetent volunteers. Coron **Artery** Dis 1994;5:943-9.
13. Blackburn H, Keys A, Simonson E, Rautaharju P, Punsar...

...Jay R, et al. Different intensities of oral anticoagulant therapy in the treatment of proximal- **vein thrombosis** . N Engl J Med 1982;307:1676-81.
15. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of **balloon** -expandable stent implantation with **balloon angioplasty** in patients with **coronary artery** disease. N Engl J Med 1994;331:489-95.
16. Serruys PW, Foley DP, de Feyter PJ, eds. Quantitative **coronary** angiography in clinical practice. Dordrecht, the Netherlands: Kluwer Academic Publishers, 1994.
17. Kalbfleisch JD, Prentice...

...Schwartz L, Bourassa MG, Lesperance J, et al. Aspirin and dipyridamole in the prevention of **restenosis** after percutaneous transluminal **coronary angioplasty** . N Engl J Med 1988;318:1714-9.
19. Chesebro JH, Webster MWI, Reeder GS, et al. **Coronary angioplasty** : antiplatelet therapy reduces acute complications but not **restenosis** . Circulation 1989;80:Suppl II:II-64. abstract.
20. Bertrand ME, Allain H, Lablanche JM. Results of a randomized trial of ticlopidine versus placebo for prevention of acute closure and **restenosis** after **coronary angioplasty** (PTCA): the TACT study. Circulation 1990;82:Suppl III:III-190. abstract.
21. Topol EJ, Califf RM, Weisman HF, et al. Randomised trial of **coronary** intervention with antibody against platelet IIb/IIIa integrin for reduction of clinical **restenosis** : results at six months. Lancet 1994;343:881-6.
22. The EPIC Investigators. Use of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk **coronary angioplasty** . N Engl J Med 1994;330:956-61.

23. Verstraete M, Nurmohamed M, Kienast J...

...8.
24. Eriksson BI, Kalebo P, Ekman S, Lindbratt S, Kerry R, Close P. Direct **thrombin** inhibition with rec-hirudin CGP 39393 as prophylaxis of **thromboembolic** complications after total hip replacement. **Thromb** Haemost 1994;72:227-31.
25. van den Bos AA, Deckers JW, Heyndrickx GR, et...

...efficacy of recombinant hirudin (CGP 39 393) versus heparin in patients with stable angina undergoing **coronary angioplasty** . Circulation 1993;88:2058-66.
26. Zoldhelyi P, Bichler J, Owen WG, et al. Persistent **thrombin** generation in humans during specific **thrombin** inhibition with hirudin. Circulation 1994;90:2671-8.
27. Chesebro JH, Badimon L, Fuster V. Importance of antithrombin therapy during **coronary angioplasty** . J Am Coll Cardiol 1991;17:Suppl B:96B-100B.
28. Wilentz JR, Sanborn TA, Haudenschild **CC** , Valeri CR, Ryan TJ, Faxon DP. Platelet accumulation in experimental **angioplasty** : time course and relation to **vascular** injury. Circulation 1987;75:636-42.
29. Groves HM, Kinlough-Rathbone RL, Mustard JF. Development of nonthrombogenicity of injured rabbit aortas despite inhibition of platelet adherence. **Arteriosclerosis** 1986;6:189-95.
30. Steele PM, Chesebro JH, Stanson AW, et al. **Balloon angioplasty** : natural history of the pathophysiological response to injury in a pig model. Circ Res 1985...

39/5,K/55 (Item 10 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00112755

Medical Progress: Percutaneous Transluminal Coronary Angioplasty **(Review Article)**

Landau, Charles; Lange, Richard A.; Hillis, L. David.
The New England Journal of Medicine
Apr 7, **1994** ; 330 (14),pp 981-993
LINE COUNT: 00661 WORD COUNT: 09123
ISSN: 0028-4793
CORPORATE SOURCE: From the Department of Internal Medicine, Cardiovascular Division, University of Texas Southwestern Medical Center, and the Cardiac Catheterization Laboratory, Parkland Memorial Hospital, Dallas. Address reprint requests to Dr. Hillis at Room CS 7.102, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75235-9047.

CITED REFERENCES
1. Dotter CT, Judkins MP. Transluminal treatment of **arteriosclerotic obstruction** : description of a new technique and a preliminary report of its application. Circulation 1964;30:654-70.
2. Gruntzig A. Transluminal dilatation of **coronary - artery stenosis** . Lancet 1978;1:263.
3. Detre K, Holubkov R, Kelsey S, et al. Percutaneous transluminal **coronary angioplasty** in 1985-1986 and 1977-1981: the National Heart, Lung, and Blood Institute Registry. N Engl J Med 1988;318:265-70.
4. Topol EJ, Ellis SG, Cosgrove DM, et al. Analysis of **coronary angioplasty** practice in the United States with an insurance-claims data base. Circulation 1993;87:1489-97.
5. Faxon DP, Weber VJ, Haudenschild C, Gottsman SB, McGovern WA, Ryan TJ. Acute effects of transluminal **angioplasty** in three experimental models of atherosclerosis. **Arteriosclerosis** 1982;2:125-33.
6. Steele PM, Chesebro JH, Stanson AW, et al. **Balloon angioplasty** : natural history of the pathophysiological response to injury in a pig model. Circ Res 1985;57:105-12.

7. Farb A, Virmani R, Atkinson JB, Kolodgie FD. **Plaque** morphology and pathologic changes in **arteries** from patients dying after **coronary balloon angioplasty** . J Am Coll Cardiol 1990;16:1421-9.
8. Soward AL, Essed CE, Serruys PW. **Coronary arterial** findings after accidental death immediately after successful percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1985;56:794-5.
9. Tenaglia AN, Buller CE, Kisslo KB, Stack RS, Davidson CJ. Mechanisms of **balloon angioplasty** and directional **coronary** atherectomy as assessed by intracoronary ultrasound. J Am Coll Cardiol 1992;20:685-91.
10. Potkin BN, Keren G, Mintz GS, et al. **Arterial** responses to **balloon coronary angioplasty** : an **intravascular** ultrasound study. J Am Coll Cardiol 1992;20:942-51.
11. Waller BF. Early and late morphologic changes in human **coronary arteries** after percutaneous transluminal **coronary angioplasty** . Clin Cardiol 1983;6:363-72.
12. Nobuyoshi M, Kimura T, Nosaka H, et al. **Restenosis** after successful percutaneous transluminal **coronary angioplasty** : serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616-23.
13. Barnathan ES, Schwartz JS, Taylor L, et al. Aspirin and dipyridamole in the prevention of acute **coronary thrombosis** complicating **coronary angioplasty** . Circulation 1987;76:125-34.
14. Schwartz L, Bourassa MG, Lesperance J, et al. Aspirin and dipyridamole in the prevention of **restenosis** after percutaneous transluminal **coronary angioplasty** . N Engl J Med 1988;318:1714-9.
15. Lembo NJ, Black AJR, Roubin GS, et al. Effect of pretreatment with aspirin versus aspirin plus dipyridamole on frequency and type of acute complications of percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1990;65:422-6.
16. Bertrand ME, Allain H, Lablanche JM, TACT Investigators. Results of a randomized trial of ticlopidine versus placebo for prevention of acute closure and **restenosis** after **coronary angioplasty** (PTCA): the TACT study. Circulation 1990;82:Suppl III:III-190. abstract.
17. McGarry TF Jr, Gottlieb RS, Morganroth J, et al. The relationship of anticoagulation level and complications after successful percutaneous transluminal **coronary angioplasty** . Am Heart J 1992;123:1445-51.
18. Gabliani G, Deligonul U, Kern MJ, Vandormael M. Acute **coronary occlusion** occurring after successful percutaneous transluminal **coronary angioplasty** : temporal relationship to discontinuation of anticoagulation. Am Heart J 1988;116:696-700.
19. Fischell TA, Derby G, Tse TM, Stadius ML. **Coronary artery** vasoconstriction routinely occurs after percutaneous transluminal **coronary angioplasty** : a quantitative **arteriographic** analysis. Circulation 1988;78:1323-34.
20. Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal **coronary angioplasty** : a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal **Coronary Angioplasty**). J Am Coll Cardiol 1988;12:529-45.
21. Popma JJ, Dehmer GJ. Care of the patient after **coronary angioplasty** . Ann Intern Med 1989;110:547-59.
22. Gruentzig AR, King SB III, Schlumpf M, Siegenthaler W. Long-term follow-up after percutaneous transluminal **coronary angioplasty** : the early Zurich experience. N Engl J Med 1987;316:1127-32.
23. Hollman J, Simpfendorfer C, Franco I, Whitlow P, Goormastic M. Multivessel and single-vessel **coronary angioplasty** : a comparative study. Am Heart J 1992;124:9-12.
24. Parisi AF, Folland ED, Hartigan P. A comparison of **angioplasty** with medical therapy in the treatment of single-vessel **coronary artery** disease. N Engl J Med 1992;326:10-6.
25. Ellis SG. Elective **coronary angioplasty** : technique and complications. In: Topol EJ, ed. Textbook of interventional cardiology. Philadelphia: W.B. Saunders, 1990:200-1.
26. Meier B. Total **coronary occlusion** : a different animal? J Am Coll Cardiol 1991;17:Suppl B:50B-57B.
27. Bell MR, Berger PB, Bresnahan JF, Reeder GS, Bailey KR, Holmes DR Jr. Initial and long-term outcome of 354 patients after **coronary balloon**

angioplasty of total **coronary artery occlusions** . Circulation 1992;85:1003-11.
28. Ivanhoe RJ, Weintraub WS, Douglas JS Jr, et al. Percutaneous transluminal **coronary angioplasty** of chronic total **occlusions** : primary success, **restenosis** , and long-term clinical follow-up. Circulation 1992;85:106-15.
29. Stone GW, Rutherford BD, McConahay DR, et al. Procedural outcome of **angioplasty** for total **coronary artery occlusion** : an analysis of 971 lesions in 905 patients. J Am Coll Cardiol 1990;15:849-56.
30. Ruocco NA Jr, Ring ME, Holubkov R, Jacobs AK, Detre KM, Faxon DP. Results of **coronary angioplasty** of chronic total **occlusions** (the National Heart, Lung, and Blood Institute 1985-1986 Percutaneous Transluminal **Angioplasty** Registry). Am J Cardiol 1992;69:69-76.
31. Killip T. Twenty years of **coronary** bypass surgery. N Engl J Med 1988;319:366-8.
32. Webb JG, Myler RK, Shaw RE, et al. **Coronary angioplasty** after **coronary** bypass surgery: initial results and late outcome in 422 patients. J Am Coll Cardiol 1990;16:812-20.
33. Platko WP, Hollman J, Whitlow PL, Franco I. Percutaneous transluminal **angioplasty** of saphenous **vein** graft **stenosis** : long-term follow-up. J Am Coll Cardiol 1989;14:1645-50.
34. de Feyter PJ, van Suylen R-J, de Jaegere PPT, Topol EJ, Serruys PW. **Balloon angioplasty** for the treatment of lesions in saphenous **vein** bypass grafts. J Am Coll Cardiol 1993;21:1539-49.
35. Urban P, Sigwart U, Golf S, Kaufmann U, Sadeghi H, Kappenberger L. **Intravascular** stenting for **stenosis** of aortocoronary **venous** bypass grafts. J Am Coll Cardiol 1989;13:1085-91.
36. Faxon DP, Ruocco N, Jacobs AK. Long-term outcome of patients after percutaneous transluminal **coronary angioplasty** . Circulation 1990;81: Suppl IV:IV-9-IV-13.
37. Bourassa MG, Holubkov R, Yeh W, Detre KM, Co-investigators of the National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. Strategy of complete revascularization in patients with multivessel **coronary artery** disease (a report from the 1985-1986 NHLBI PTCA Registry). Am J Cardiol 1992;70:174-8.
38. Wohlgelernter D, Cleman M, Highman HA, Zaret BL. Percutaneous transluminal **coronary angioplasty** of the ``culprit lesion'' for management of unstable angina pectoris in patients with multivessel **coronary artery** disease. Am J Cardiol 1986;58:460-4.
39. King SB III, Lembo NJ, Hall EC, EAST Investigators. The Emory **Angioplasty** vs. Surgery Trial (EAST): analysis of baseline patient characteristics. Circulation 1990;82:Suppl III:III-508. abstract.
40. Rodriguez A, Boullon F, Perez-Balino N, Paviotti C, Sosa Liprandi MI, Palacios IF. Argentine randomized trial of percutaneous transluminal **coronary angioplasty** versus **coronary artery** bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. J Am Coll Cardiol 1993;22:1060-7.
41. Landau C, Faxon DP. Acronyms in **angioplasty** and **restenosis** : a summary of recent and ongoing clinical randomized trials. J Interv Cardiol 1992;5:29-37.
42. RITA Trial Participants. **Coronary angioplasty** versus **coronary artery** bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. Lancet 1993;341:573-80.
43. Leeman DE, McCabe CH, Faxon DP, et al. Use of percutaneous transluminal **coronary angioplasty** and bypass surgery despite improved medical therapy for unstable angina pectoris. Am J Cardiol 1988;61:38G-44G.
44. Mulcahy R, Al Awadhi AH, de Buitleor M, Tobin G, Johnson H, Contoy R. Natural history and prognosis of unstable angina. Am Heart J 1985;109:753-8.
45. Theroux P, Ouimet H, McCans J, et al. Aspirin, heparin, or both to treat acute unstable angina. N Engl J Med 1988;319:1105-11.
46. Grambow DW, Topol EJ. Effect of maximal medical therapy on refractoriness of unstable angina pectoris. Am J Cardiol 1992;70:577-81.
47. de Feyter PJ, Serruys PW, van den Brand M, et al. Emergency **coronary angioplasty** in refractory unstable angina. N Engl J Med 1985;313:342-6.

48. Stammen F, De Scheerder I, Glazier JJ, et al. Immediate and follow-up results of the conservative **coronary angioplasty** strategy for unstable angina pectoris. Am J Cardiol 1992;69:1533-7.
49. Myler RK, Shaw RE, Stertzer SH, et al. Unstable angina and **coronary angioplasty** . Circulation 1990;82:Suppl II:II-88-II-95.
50. de Feyter PJ, Serruys PW, v d Brand M, Hugenholtz PG. Percutaneous transluminal **coronary angioplasty** for unstable angina. Am J Cardiol 1991;68:Suppl:125B-135B.
51. Holmes DR Jr, Holubkov R, Vlietstra RE, et al. Comparison of complications during percutaneous transluminal **coronary angioplasty** from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. J Am Coll Cardiol 1988;12:1149-55.
52. Lambert M, Bonan R, Cote G, et al. Multiple **coronary angioplasty** : a model to discriminate systemic and procedural factors related to **restenosis** . J Am Coll Cardiol 1988;12:310-4.
53. Leimgruber PP, Roubin GS, Hollman J, et al. **Restenosis** after successful **coronary angioplasty** in patients with single-vessel disease. Circulation 1986;73:710-7.
54. Laskey MAL, Deutsch E, Barnathan E, Laskey WK. Influence of heparin therapy on percutaneous transluminal **coronary angioplasty** outcome in unstable angina pectoris. Am J Cardiol 1990;65:1425-9.
55. Perry RA, Seth A, Hunt A, Shiu MF. **Coronary angioplasty** in unstable angina and stable angina: a comparison of success and complications. Br Heart J 1988;60:367-72.
56. Ambrose JA, Torre SR, Sharma SK, et al. Adjunctive **thrombolytic** therapy for **angioplasty** in **ischemic** rest angina: results of a double-blind randomized pilot study. J Am Coll Cardiol 1992;20:1197-204.
57. Grines CL, Browne KF, Marco J, et al. A comparison of immediate **angioplasty** with **thrombolytic** therapy for acute myocardial infarction. N Engl J Med 1993;328:673-9.
58. Zijlstra F, de Boer MJ, Hoorntje JCA, Reiffers S, Reiber JHC, Suryapranata H. A comparison of immediate **coronary angioplasty** with **intravenous** streptokinase in acute myocardial infarction. N Engl J Med 1993;328:680-4.
59. Gibbons RJ, Holmes DR, Reeder GS, et al. Immediate **angioplasty** compared with the **administration** of a **thrombolytic** agent followed by conservative treatment for myocardial infarction. N Engl J Med 1993;328:685-91.
60. Landau C, Glamann DB, Willard JE, Hillis LD, Lange RA. **Coronary angioplasty** in the patient with acute myocardial infarction. Am J Med (in press).
61. Neuhaus KL, Von Essen R, Tebbe U, et al. Improved **thrombolysis** in acute myocardial infarction with front-loaded **administration** of alteplase: results of the rt-PA-APSAC patency study (TAPS). J Am Coll Cardiol 1992;19:885-91.
62. Topol EJ, Califf RM, George BS, et al. A randomized trial of immediate versus delayed elective **angioplasty** after **intravenous** tissue plasminogen activator in acute myocardial infarction. N Engl J Med 1987;317:581-8.
63. TIMI Research Group. Immediate vs delayed **catheterization** and **angioplasty** following **thrombolytic** therapy for acute myocardial infarction: TIMI II A results. JAMA 1988;260:2849-58.
64. Simoons ML, Arnold AER, Betriu A, et al. **Thrombolysis** with tissue plasminogen activator in acute myocardial infarction: no additional benefit from immediate percutaneous **coronary angioplasty** . Lancet 1988;1:197-203.
65. Arnold AER, Simoons ML, Van de Werf F, et al. Recombinant tissue-type plasminogen activator and immediate **angioplasty** in acute myocardial infarction: one-year follow-up. Circulation 1992;86:111-20.
66. O'Neill WW, Weintraub R, Grines CL, et al. A prospective, placebo-controlled, randomized trial of **intravenous** streptokinase and **angioplasty** versus lone **angioplasty** therapy of acute myocardial infarction. Circulation 1992;86:1710-7.
67. SWIFT (Should We Intervene Following **Thrombolysis** ?) Trial Study Group. SWIFT trial of delayed elective intervention v conservative treatment after **thrombolysis** with anistreplase in acute myocardial

infarction. BMJ 1991;302:555-60.
68. TIMI Study Group. Comparison of invasive and conservative strategies after treatment with **intravenous** tissue plasminogen activator in acute myocardial infarction: results of the **Thrombolysis** in Myocardial Infarction (TIMI) phase II trial. N Engl J Med 1989;320:618-27.
69. Williams DO, Braunwald E, Knatterud G, et al. One-year results of the **Thrombolysis** in Myocardial Infarction Investigation (TIMI) phase II trial. Circulation 1992;85:533-42.
70. Cowley MJ, Dorros G, Kelsey SF, Van Raden M, Detre KM. Acute **coronary** events associated with percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1984;53:12C-16C.
71. Talley JD, Weintraub WS, Roubin GS, et al. Failed elective percutaneous transluminal **coronary angioplasty** requiring **coronary artery** bypass surgery: in-hospital and late clinical outcome at 5 years. Circulation 1990;82:1203-13.
72. Hartz AJ, Kuhn EM, Pryor DB, et al. Mortality after **coronary angioplasty** and **coronary artery** bypass surgery (the national Medicare experience). Am J Cardiol 1992;70:179-85.
73. Myler RK, Shaw RE, Stertzer SH, et al. Lesion morphology and **coronary angioplasty** : current experience and analysis. J Am Coll Cardiol 1992;19:1641-52.
74. Ellis SG, Roubin GS, King SB III, et al. Angiographic and clinical predictors of acute closure after native vessel **coronary angioplasty** . Circulation 1988;77:372-9.
75. Simpfendorfer C, Balardi J, Bellamy G, Galan K, Franco I, Hollman J. Frequency, management and follow-up of patients with acute **coronary occlusions** after percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1987;59:267-9.
76. Sinclair IN, McCabe CH, Sipperly ME, Baim DS. Predictors, therapeutic options and long-term outcome of abrupt reclosure. Am J Cardiol 1988;61:61G-66G.
77. Lincoff AM, Popma JJ, Ellis SG, Hacker JA, Topol EJ. Abrupt vessel closure complicating **coronary angioplasty** : clinical, angiographic and therapeutic profile. J Am Coll Cardiol 1992;19:926-35.
78. Mabin TA, Holmes DR Jr, Smith HC, et al. Intracoronary **thrombus** : role in **coronary occlusion** complicating percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1985;5:198-202.
79. Bredlau CE, Roubin GS, Leimgruber PP, Douglas JS Jr, King SB III, Gruentzig AR. In-hospital morbidity and mortality in patients undergoing elective **coronary angioplasty** . Circulation 1985;72:1044-52.
80. Detre KM, Holmes DR Jr, Holubkov R, et al. Incidence and consequences of periprocedural **occlusion** : the 1985-1986 National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. Circulation 1990;82:739-50.
81. de Feyter PJ, van den Brand M, Laarman GJ, et al. Acute **coronary artery occlusion** during and after percutaneous transluminal **coronary angioplasty** : frequency, prediction, clinical course, management, and follow-up. Circulation 1991;83:927-36.
82. Ellis SG, Topol EJ. Results of percutaneous transluminal **coronary angioplasty** of high-risk angulated **stenoses** . Am J Cardiol 1990;66:932-7.
83. Savage MP, Goldberg S, Hirshfeld JW, et al. Clinical and angiographic determinants of primary **coronary angioplasty** success. J Am Coll Cardiol 1991;17:22-8.
84. Roubin GS, Douglas JS Jr, King SB III, et al. Influence of **balloon** size on initial success, acute complications, and **restenosis** after percutaneous transluminal **coronary angioplasty** : a prospective randomized study. Circulation 1988;78:557-65.
85. Leitschuh ML, Mills RM Jr, Jacobs AK, Ruocco NA Jr, LaRosa D, Faxon DP. Outcome after major dissection during **coronary angioplasty** using the perfusion **balloon catheter** . Am J Cardiol 1991;67:1056-60.
86. Van Lierde JM, Glazier JJ, Stammen FJ, et al. Use of an autoperfusion **catheter** in the treatment of acute refractory vessel closure after **coronary balloon angioplasty** : immediate and six month follow up results. Br Heart J 1992;68:51-4.
87. Roubin GS, Cannon AD, Agrawal SK, et al. Intracoronary stenting for

acute and threatened closure complicating percutaneous transluminal **coronary angioplasty** . Circulation 1992;85:916-27.
88. Lincoff AM, Topol EJ, Chapekis AT, et al. Intracoronary stenting compared with conventional therapy for abrupt vessel closure complicating **coronary angioplasty** : a matched case-control study. J Am Coll Cardiol 1993;21:866-75.
89. Schieman G, Cohen BM, Kozina J, et al. Intracoronary urokinase for intracoronary **thrombus** accumulation complicating percutaneous transluminal **coronary angioplasty** in acute **ischemic** syndromes. Circulation 1990;82:2052-60.
90. Lee TC, Hartzler GO, Rutherford BD, McConahay DR. Removal of an **occlusive coronary** dissection flap by using an atherectomy **catheter** . Cathet Cardiovasc Diagn 1990;20:185-8.
91. Lazar HL, Faxon DP, Paone G, et al. Changing profiles of failed **coronary angioplasty** patients: impact on surgical results. Ann Thorac Surg 1992;53:269-73.
92. Landau C, Jacobs AK, Yeh W, et al. Long term follow-up of patients undergoing emergent CABG in the 1985-1986 NHLBI PTCA Registry. Circulation 1991;84:Suppl II:II-291. abstract.
93. Muller DWM, Shamir KJ, Ellis SG, Topol EJ. Peripheral **vascular** complications after conventional and complex percutaneous **coronary** interventional procedures. Am J Cardiol 1992;69:63-8.
94. Oweida SW, Roubin GS, Smith RB III, Salam AA. Postcatheterization **vascular** complications associated with percutaneous transluminal **coronary angioplasty** . J Vasc Surg 1990;12:310-5.
95. Wyman RM, Safian RD, Portway V, Skillman JJ, McKay RG, Baim DS. Current complications of diagnostic and therapeutic cardiac **catheterization** . J Am Coll Cardiol 1988;12:1400-6.
96. Landau C, Lange RA, Glamann DB, Willard JE, Hillis LD. Vasovagal reactions in the cardiac **catheterization** laboratory. Am J Cardiol 1994;73:95-7.
97. MERCATOR Study Group. Does the new angiotensin converting enzyme inhibitor cilazapril prevent **restenosis** after percutaneous transluminal **coronary angioplasty** ? Results of the MERCATOR study: a multicenter, randomized, double-blind placebo-controlled trial. Circulation 1992;86:100-10.
98. Hirshfeld JW Jr, Schwartz JS, Jugo R, et al. **Restenosis** after **coronary angioplasty** : a multivariate statistical model to relate lesion and procedure variables to **restenosis** . J Am Coll Cardiol 1991;18:647-56.
99. Lange RA, Willard JE, Hillis LD. **Restenosis** : the Achilles heel of **coronary angioplasty** . Am J Med Sci 1993;306:265-75.
100. Libby P, Schwartz D, Brogi E, Tanaka H, Clinton SK. A cascade model for **restenosis** : a special case of atherosclerosis progression. Circulation 1992;86:Suppl III:III-47-III-52.
101. Haudenschild **CC** . Pathobiology of **restenosis** after **angioplasty** . Am J Med 1993;94:Suppl 4A:4A-40S-4A-44S.
102. Haude M, Erbel R, Issa H, Meyer J. Quantitative analysis of elastic recoil after **balloon angioplasty** and after intracoronary implantation of **balloon** -expandable Palmaz-Schatz stents. J Am Coll Cardiol 1993;21:26-34.
103. Holmes DR Jr, Vlietstra RE, Smith HC, et al. **Restenosis** after percutaneous transluminal **coronary angioplasty** (PTCA): a report from the PTCA Registry of the National Heart, Lung, and Blood Institute. Am J Cardiol 1984;53:Suppl:77C-81C.
104. Galan KM, Deligonul U, Kern MJ, Chaitman BR, Vandormael MG. Increased frequency of **restenosis** in patients continuing to smoke cigarettes after percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1988;61:260-3.
105. Austin GE, Lynn M, Hollman J. Laboratory test results as predictors of recurrent **coronary artery stenosis** following **angioplasty** . Arch Pathol Lab Med 1987;111:1158-62.
106. Weintraub WS, Kosinski AS, Brown CL III, King SB III. Can **restenosis** after **coronary angioplasty** be predicted from clinical variables? J Am Coll Cardiol 1993;21:6-14.
107. Reis GJ, Kuntz RE, Silverman DI, Pasternak RC. Effects of serum lipid levels on **restenosis** after **coronary angioplasty** . Am J Cardiol 1991;68:1431-5.

108. Kahn JK, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Hartzler GO. Short- and long-term outcome of percutaneous transluminal **coronary angioplasty** in chronic dialysis patients. Am Heart J 1990;119:484-9.

109. Guiteras Val P, Bourassa MG, David PR, et al. **Restenosis** after successful percutaneous transluminal **coronary angioplasty** : the Montreal Heart Institute experience. Am J Cardiol 1987;60:Suppl:50B-55B.
110. Leisch F, Schutzenberger W, Kerschner K, Herbinger W. Influence of a variant angina on the results of percutaneous transluminal **coronary angioplasty** . Br Heart J 1986;56:341-5.
111. Black AJR, Anderson HV, Roubin GS, Powelson SW, Douglas JS Jr, King SB III. Repeat **coronary angioplasty** : correlates of a second **restenosis** . J Am Coll Cardiol 1988;11:714-8.
112. Quigley PJ, Hlatky MA, Hinohara T, et al. Repeat percutaneous transluminal **coronary angioplasty** and predictors of recurrent **restenosis** . Am J Cardiol 1989;63:409-13.
113. Vandormael MG, Deligonul U, Kern MJ, et al. Multilesion **coronary angioplasty** : clinical and angiographic follow-up. J Am Coll Cardiol 1987;10:246-52.
114. Roubin GS, King SB III, Douglas JS Jr. **Restenosis** after percutaneous transluminal **coronary angioplasty** : the Emory University Hospital experience. Am J Cardiol 1987;60:Suppl:39B-43B.
115. Bourassa MG, Lesperance J, Eastwood C, et al. Clinical, physiologic, anatomic and procedural factors predictive of **restenosis** after percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1991;18:368-76.
116. Kuntz RE, Gibson CM, Nobuyoshi M, Baim DS. Generalized model of **restenosis** after conventional **balloon angioplasty** , stenting and directional atherectomy. J Am Coll Cardiol 1993;21:15-25.
117. Nichols AB, Smith R, Berke AD, Shlofmitz RA, Powers ER. Importance of **balloon** size in **coronary angioplasty** . J Am Coll Cardiol 1989;13:1094-100.
118. Hernandez RA, Macaya C, Iniguez A, et al. Midterm outcome of patients with asymptomatic **restenosis** after **coronary balloon angioplasty** . J Am Coll Cardiol 1992;19:1402-9.
119. Foley DP, Hermans WR, Rutsch W, et al. **Restenosis** after PTCA affects the entire vessel segment dilated. J Am Coll Cardiol 1993;21:Suppl A: 322A. abstract.
120. Chesebro JH, Webster MW, Reeder GS, et al. **Coronary angioplasty** : antiplatelet therapy reduces acute complications but not **restenosis** . Circulation 1989;80:Suppl II:II-64. abstract.
121. Knudtson ML, Flintoft VF, Roth DL, Hansen JL, Duff HJ. Effect of short-term prostacyclin administration on **restenosis** after percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1990;15:691-7.
122. Raizner A, Hollman J, Demke D, Wakefield L, Ciprostene Investigators. Beneficial effects of ciprostene in PTCA: a multicenter, randomized, controlled trial. Circulation 1988;78:Suppl II:II-290. abstract.
123. Serruys PW, Rutsch W, Heyndrickx GR, et al. Prevention of **restenosis** after percutaneous transluminal **coronary angioplasty** with **thromboxane** A2-receptor blockade: a randomized, double-blind, placebo-controlled trial: **Coronary Artery Restenosis** Prevention on Repeated **Thromboxane** -Antagonism Study (CARPORT). Circulation 1991;84:1568-80.
124. Klein W, Eber B, Dusleag J, et al. Ketanserin prevents early **restenosis** following percutaneous transluminal **coronary angioplasty** . Clin Physiol Biochem 1990;8:Suppl 3:101-7.
125. Serruys PW, Klein W, Rutsch W, et al. PARK: the Post **Angioplasty Restenosis** Ketanserin trial. J Am Coll Cardiol 1993;21:Suppl A:322A. abstract.
126. Ellis SG, Roubin GS, Wilentz J, Douglas JS Jr, King SB III. Effect of 18- to 24-hour heparin administration for prevention of **restenosis** after uncomplicated **coronary angioplasty** . Am Heart J 1989;117:777-82.
127. Thornton MA, Gruentzig AR, Hollman J, King SB III, Douglas JS. Coumadin and aspirin in prevention of recurrence after transluminal **coronary angioplasty** : a randomized study. Circulation 1984;69:721-7.

128. Urban P, Buller N, Fox K, Shapiro L, Bayliss J, Rickards A. Lack of effect of warfarin on the **restenosis** rate or on clinical outcome after **balloon coronary angioplasty** . Br Heart J 1988;60:485-8.
129. Whitworth HB, Roubin GS, Hollman J, et al. Effect of nifedipine on recurrent **stenosis** after percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1986;8:1271-6.
130. O'Keefe JH Jr, Giorgi LV, Hartzler GO, et al. Effects of diltiazem on complications and **restenosis** after **coronary angioplasty** . Am J Cardiol 1991;67:373-6.
131. Corcos T, David PR, Val PG, et al. Failure of diltiazem to prevent **restenosis** after percutaneous transluminal **coronary angioplasty** . Am Heart J 1985;109:926-31.
132. Pepine CJ, Hirshfeld JW, Macdonald RG, et al. A controlled trial of corticosteroids to prevent **restenosis** after **coronary angioplasty** : M-HEART Group. Circulation 1990;81:1753-61.
133. O'Keefe JH Jr, McCallister BD, Bateman TM, Kuhnlein DL, Ligon RW, Hartzler GO. Ineffectiveness of colchicine for the prevention of **restenosis** after **coronary angioplasty** . J Am Coll Cardiol 1992;19:1597-600.
134. Dehmer GJ, Popma JJ, van den Berg EK, et al. Reduction in the rate of early **restenosis** after **coronary angioplasty** by a diet supplemented with n-3 fatty acids. N Engl J Med 1988;319:733-40.
135. Milner MR, Gallino RA, Leffingwell A, et al. Usefulness of fish oil supplements in preventing clinical evidence of **restenosis** after percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1989;64:294-9.
136. Reis GJ, Boucher TM, Sipperly ME, et al. Randomised trial of fish oil for prevention of **restenosis** after **coronary angioplasty** . Lancet 1989;2:177-81.
137. Grigg LE, Kay TWH, Valentine PA, et al. Determinants of **restenosis** and lack of effect of dietary supplementation with eicosapentaenoic acid on the incidence of **coronary artery restenosis** after **angioplasty** . J Am Coll Cardiol 1989;13:665-72.
138. Bairati I, Roy L, Meyer F. Double-blind, randomized, controlled trial of fish oil supplements in prevention of recurrence of **stenosis** after **coronary angioplasty** . Circulation 1992;85:950-6.
139. Sahni R, Maniet AR, Voci G, Banka VS. Prevention of **restenosis** by lovastatin after successful **coronary angioplasty** . Am Heart J 1991;121:1600-8.
140. Hollman J, Konrad K, Raymond R, Whitlow P, Michalak M, Van Lente F. Lipid lowering for the prevention of recurrent **stenosis** following **coronary angioplasty** . Circulation 1989;80:Suppl II:II-65. abstract.
141. Okamoto S, Inden M, Setsuda M, Konishi T, Nakano T. Effects of trapidil (triazolopyrimidine), a platelet-derived growth factor antagonist, in preventing **restenosis** after percutaneous transluminal **coronary angioplasty** . Am Heart J 1992;123:1439-44.
142. Serruys PW, Strauss BH, Beatt KJ, et al. Angiographic follow-up after placement of a self-expanding **coronary - artery** stent. N Engl J Med 1991;324:13-7.
143. Kimura T, Nosaka H, Yokoi H, Iwabuchi M, Nobuyoshi M. Serial angiographic follow-up after Palmaz-Schatz stent implantation: comparison with conventional **balloon angioplasty** . J Am Coll Cardiol 1993;21:1557-63.
144. Safian RD, Gelbfish JS, Erny RE, Schnitt SJ, Schmidt DA, Baim DS. **Coronary** atherectomy: clinical, angiographic, and histological findings and observations regarding potential mechanisms. Circulation 1990;82:69-79.
145. Hillis LD. Efficacy and safety of **coronary balloon angioplasty** and directional atherectomy. Circulation 1990;82:305-7.
146. Popma JJ, Topol EJ, Hinohara T, et al. Abrupt vessel closure after directional **coronary** atherectomy. J Am Coll Cardiol 1992;19:1372-9.
147. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of directional atherectomy with **coronary angioplasty** in patients with **coronary artery** disease. N Engl J Med 1993;329:221-7.
148. Adelman AG, Cohen EA, Kimball BP, et al. A comparison of directional atherectomy with **balloon angioplasty** for lesions of the left anterior descending **coronary artery** . N Engl J Med 1993;329:228-33.

149. Cohen DJ, Breall JA, Ho KKL, et al. Economics of elective **coronary** revascularization: comparison of costs and charges for conventional **angioplasty** , directional atherectomy, stenting and bypass surgery. J Am Coll Cardiol 1993;22:1052-9.
150. Black AJR, Roubin GS, Sutor C, et al. Comparative costs of percutaneous transluminal **coronary angioplasty** and **coronary artery** bypass grafting in multivessel **coronary artery** disease. Am J Cardiol 1988;62:809-11. □

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

Medical Progress: Percutaneous Transluminal Coronary Angioplasty **(Review Article)**
1994 ;

TEXT
...The nonsurgical treatment of **arteries** narrowed by atherosclerosis was introduced in 1964, when Dotter and Judkins performed transluminal **angioplasty** of femoral **arterial stenoses** (Ref. 1). In the 1970s, Gruntzig modified the dilation **catheter** to allow its use in **coronary arteries** , (Ref. 2) and in September 1977 he performed the first percutaneous transluminal **coronary angioplasty** (PTCA) in a patient. PTCA has since been used in many patients with stable angina...

...angina, or acute myocardial infarction. Its use was initially limited to the treatment of discrete **stenoses** in proximal segments of a **coronary artery** , but improvements in equipment and technique have led to its use in patients with **stenoses** that are more complex or located in distal **arterial** segments and in patients at relatively high risk for complications (Ref. 3). Despite the wider...

...Mechanisms of **Arterial** Dilation
The mechanisms by which PTCA increases the size of the **arterial lumen** have been studied in animals and cadavers. **Balloon** -induced barotrauma causes endothelial denudation; cracking, splitting, and disruption of the atherosclerotic **plaque** ; dehiscence of the intima and **plaque** from the underlying media; and stretching or tearing of the media and adventitia, with resultant aneurysmal dilatation (Fig. 1) (Ref. 5,6). **Plaque** fissuring, medial and adventitial stretching, and separation of the atheroma from the underlying media account...

...dissection (Ref. 7,8). Intracoronary ultrasound imaging, which provides a cross-sectional view of the **artery** from within the **lumen** , has provided in vivo confirmation of these morphologic findings after PTCA. With ultrasound imaging, dissection of the **arterial** wall -- at times extensive -- is detected in 50 to 80 percent of patients who have...

...morphologic alterations open up new pathways for blood flow, leading to an increased luminal size. **Balloon inflation** may be deleterious, however, causing **plaque** hemorrhage, extensive dissection (resulting in luminal compromise), platelet deposition, or **thrombus** formation (Ref. 6,11). Aspirin and heparin are administered to reduce the incidence of platelet deposition and **thrombosis** , respectively. *Figure 1.-Cross Section of a **Coronary Artery** before (Left) and after (Right) Successful PTCA. After the **balloon** has been **inflated** , the **lumen** is enlarged by fissuring of the **plaque** (1), separation of the **plaque** from the underlying layers (2), and stretching of the less diseased portion of the **artery** (3) *. **FIGURE OMITTED...

...In the weeks after successful PTCA, favorable remodeling of the disrupted **plaque** and endothelialization at the sites of intimal injury result in an increased luminal size. Angiographic...

...mg per day) is given before and after PTCA to prevent abrupt closure of the **artery** being dilated (Ref. 13,14). Dipyridamole provides no additional benefit (Ref. 15). For the patient...

...obtain the maximal antiplatelet effect. Heparin (typically 10,000 to 15,000 units) is administered **intravenously** during the procedure to

decrease the incidence of **coronary arterial thrombosis** (Ref. 17,18). The adequacy of anticoagulation is monitored in the **catheterization** laboratory by measurement of the activated clotting time. Nitroglycerin (sublingual, intracoronary, or both) and, at times, a calcium antagonist are given to prevent **coronary** vasospasm (Ref. 19) and to diminish **ischemia** during **inflation** of the **balloon** (by reducing myocardial oxygen demand while the **coronary** flow is interrupted).

The Procedure

Successful PTCA requires a skilled operator and competent cardiothoracic surgical support (Ref. 20). High-resolution fluoroscopic equipment is needed for adequate visualization of the **coronary arteries** . The procedure is performed with a special apparatus consisting of a large- **lumen** guide **catheter** , a flexible guide wire, and a **balloon catheter** . **Vascular** access is usually attained through the femoral **artery** , where a sheath is introduced with the use of local anesthesia. A 6- to 9-French guide **catheter** (2 to 3 mm in diameter) is advanced through the sheath to the ostium of the **coronary artery** to be dilated (Fig. 2A). The guide **catheter** is stiffer than the **catheters** used for diagnostic angiography, and it has a larger internal diameter to permit the passage of radiographic contrast material and visualization of the **artery** when the guide wire and **balloon catheter** are within the guide **catheter** . *Figure 2.-Procedure Used In PTCA. The guide **catheter** is introduced through a femoral **arterial** sheath and advanced to the ostium of the diseased **coronary artery** (Panel A). The guide wire is advanced through the central **lumen** of the **balloon catheter** into the diseased **artery** and across the **stenosis** (Panel B). The **balloon** is slid forward over the guide wire, positioned adjacent to the **stenosis** , and **inflated** (Panel C). After one or more **inflations** , the guide wire and **balloon catheter** are removed, and a final angiogram is obtained (Panel D) *. **FIGURE OMITTED...

...With the guide **catheter** positioned in the **coronary** ostium, angiography of the diseased **artery** is performed to visualize the **stenosis** and the **arterial** segments proximal and distal to it. The flexible guide wire (0.25 to 0.46 mm in diameter) is advanced through the guide **catheter** , navigated across the **stenosis** , and positioned in the distal **arterial** segment (Fig. 2B). The guide wire is navigated by rotating and advancing its angulated tip. With the guide wire across the **stenosis** , the deflated **balloon catheter** is advanced over the wire and positioned at the **stenosis** . The positions of the guide wire and **balloon catheter** are confirmed periodically by visualization of the **artery** as contrast material is injected through the guide **catheter** . Once positioned, the **balloon** is usually **inflated** for one to two minutes at 3 to 8 atmospheres of pressure with a mixture of saline and contrast material, so that the **inflation** can be visualized fluoroscopically (Fig. 2C). Occasionally, other **inflation** variables are used. Many patients have angina, electrocardiographic evidence of **ischemia** , or both during **inflation** of the **balloon** , since the **coronary artery** is temporarily **occluded** . If the **stenosis** is adequately dilated, the guide wire and **balloon catheter** are removed. If the dilation is not adequate, the guide wire remains across the **stenosis** , and the **balloon catheter** may be replaced by a larger one. When the **inflation** has been completed, a final angiogram is obtained to confirm that the result is satisfactory and that other segments of the **artery** , including branches, have not been compromised (Fig. 2D).

Management after PTCA

The patient is observed...

...to eight hours after PTCA, while the anticoagulant effect of the heparin subsides. The femoral **arterial** sheath is then removed, and hemostasis is achieved by compression of the puncture site. The...

...remains in bed for 8 to 24 hours. If there is angiographic evidence of extensive **coronary arterial** dissection or **thrombosis** , some operators continue the heparin for 12 to 24 hours (Ref. 18). If the procedure...

...Efficacy of the Procedure

With modern equipment, PTCA of a nonoccluded **coronary artery** is successful in about 90 percent of patients, (Ref. 3,22-24) with success

defined...

...on the post-PTCA angiogram. In 10 percent of patients, PTCA is unsuccessful because the **stenosis** cannot be crossed with either the guide wire or the **balloon catheter** , the **stenosis** is not adequately dilated despite the use of a **balloon** of appropriate size, or the vessel abruptly **occludes** (abrupt closure). PTCA has a lower success rate with **stenoses** that are long, eccentric, angulated, calcified, located at the ostium or the site of a branch point, or associated with intraluminal **thrombus** (Ref. 20). The success rate is lower in patients with unstable angina or advanced age...
...PTCA has a lower initial success rate (65 to 70 percent) in patients with chronically **occluded arteries** than in those with narrowed **arteries** , since it may be difficult to manipulate the guide wire through an **occluded** region. In some cases, the guide wire can be gently advanced through an **occluding thrombus** , presumably because it is incompletely organized. In addition, the incidence of **restenosis** is higher after PTCA of an **occluded artery** (Ref. 26,27). Unlike **restenosis** after PTCA of a narrowed **artery** , **restenosis** after PTCA of an **occluded artery** is manifested as a recurrent **occlusion** in about one third of patients (Ref. 28). PTCA of **occluded arteries** is most likely to be successful in vessels that have **occluded** recently (within one to three months) and in those in which the **occlusion** is short, tapered, not calcified, and not bridged by collateral vessels (Ref. 27,29,30...

...In patients with recurrent angina after bypass surgery, PTCA of narrowed saphenous- **vein** grafts is often considered, since the perioperative mortality associated with a second bypass operation is higher than that associated with the initial operation (Ref. 31). Among patients with properly selected **vein** grafts, the success rate and frequency of acute complications are similar to those among patients with diseased native **arteries** , but the incidence of **restenosis** and late events (myocardial infarction, additional bypass surgery, or death) is higher in patients with diseased **vein** grafts (Ref. 32-34). Although the rate of **restenosis** in saphenous- **vein** grafts may be reduced by the placement of a stent, (Ref. 35) direct comparisons of this procedure with PTCA alone are lacking. PTCA of a **vein** graft is most likely to be successful in a narrowed graft implanted less than three years earlier, in which the **stenosis** is not located near the ostium and is focal rather than diffuse (Ref. 32,33...

...should be reserved for patients with angina or objective evidence of spontaneous or provocable myocardial **ischemia** .

Stable Angina on Exertion

PTCA provides effective relief of stable angina in most patients with single-vessel **coronary artery** disease (Ref. 22,24). In those with multivessel disease, the procedure is less likely to result in complete, long-term alleviation of angina, (Ref. 23,36) since the risk of **restenosis** is increased when more than one **stenosis** is dilated in a patient, and revascularization is incomplete when only ``culprit'' **stenoses** -- those deemed most likely to be responsible for symptoms -- are dilated (Ref. 37,38). Culprit **stenoses** are usually identified by noninvasive means (**radionuclide perfusion** imaging, echocardiography with provocation of myocardial **ischemia** , or electrocardiography during pain) in combination with the angiographic characteristics of the **stenosis** .

...
...PTCA and medical therapy or bypass surgery for the treatment of stable angina. In the **Angioplasty** Compared to Medicine (ACME) trial, (Ref. 24) 212 patients with stable angina, provocable myocardial **ischemia** , and single-vessel **coronary artery** disease were randomly assigned to treatment with PTCA or medical therapy. Although the initial success...

...frequency of myocardial infarction (4 percent) and emergency bypass surgery (2 percent) associated with the **angioplasty** . Since PTCA occasionally results in an adverse outcome, its risk and potential benefit as compared...

...comparing PTCA with bypass surgery in patients with stable angina and single-vessel or multivessel **coronary artery** disease are in progress,

including the Emory **Angioplasty** vs. Surgery Trial, (Ref. 39) the **Coronary Artery** Bypass Revascularization Intervention, the Argentine Randomized Trial of **Coronary Angioplasty** versus Bypass Surgery in Multiple Vessel Disease (ERACI), (Ref. 40) the German **Angioplasty** Bypass Investigation, (Ref. 41) the Randomised Intervention Treatment of Angina (RITA), (Ref. 42) and the Bypass **Angioplasty** Revascularization Investigation (Ref. 41). In a trial that enrolled 1011 patients and followed them for...
...PTCA were more likely to have angina, to require antianginal medications, and to undergo additional **coronary** angiography and revascularization (Ref. 42). Similar results after one year of follow-up were reported...

...medical therapy (Ref. 43,46). Those with angina that persists despite medical therapy usually undergo **coronary** angiography and revascularization (Ref. 43,47). The initial success rate with PTCA is slightly lower...

...angina, (Ref. 3,48,49) and the incidence of abrupt closure (Ref. 48-51) and **restenosis** (Ref. 52,53) is somewhat higher. Some studies have suggested that the incidence of abrupt...

...preferably for 10 to 14 days after the resolution of symptoms), (Ref. 49,55) or **administering intravenous thrombolytic** therapy shortly before, during, and possibly after PTCA (Ref. 56). The usefulness of PTCA in patients with unstable angina is being assessed in the **Thrombolysis** in Myocardial Infarction (TIMI) study, phase IIIB, in which patients were assigned to treatment with **coronary** angiography and revascularization or to more conservative treatment, with invasive procedures performed only when clinically...year survival rate of 90 to 96 percent. In three randomized trials comparing PTCA with **intravenous thrombolytic** therapy in patients with evolving infarction, (Ref. 57-59) anterograde flow in the infarct-related **artery** was restored in about 95 percent of the patients undergoing PTCA -- a higher percentage than that in the group of patients who received **thrombolytic** therapy (Ref. 57-59). These trials are reviewed elsewhere (Ref. 60). The patients undergoing PTCA...

...events in the hospital (nonfatal reinfarction or death) and were less likely to have recurrent **ischemia** or to require **coronary** revascularization during follow-up. As compared with **thrombolytic** therapy, PTCA was particularly advantageous in patients considered to be at high risk (those over...

...with cardiogenic shock have a markedly improved outcome if the patency of the infarct-related **artery** is restored by means of emergency PTCA (Ref. 60). The benefit of this therapeutic strategy is being evaluated in a multicenter, prospective, randomized trial.

After **Thrombolytic** Therapy

Although **thrombolytic** therapy restores anterograde **perfusion** of the **artery** in 75 to 90 percent of patients, (Ref. 61-63) some have severe residual **stenosis** , which may lead to recurrent **thrombotic occlusion** . If performed soon after **thrombolysis** , PTCA can reduce the severity of the residual **stenosis** and the likelihood of recurrent **occlusion** , thereby improving morbidity and mortality. However, several trials have demonstrated that PTCA performed immediately after **intravenous thrombolytic** therapy is not beneficial and may be deleterious. In the first phase of the **Thrombolysis** and **Angioplasty** in Myocardial Infarction (TAMI) study (Ref. 62) and in phase IIA of the TIMI study...

...had a higher incidence of bleeding complications. In TIMI IIA, those undergoing PTCA immediately after **thrombolytic** therapy had an increased incidence of combined serious adverse events (death, recurrent infarction, bypass surgery...

...Cooperative Study Group trial, (Ref. 64) the performance of PTCA immediately after the administration of **intravenous** plasminogen activator did not influence the size of the infarct or the incidence of subsequent reinfarction but did result in an increased incidence of recurrent

ischemia , bleeding complications, and blood transfusions. In addition, mortality was higher at two weeks and at...

...noted increased morbidity and no advantage when PTCA was performed immediately after the administration of **intravenous** streptokinase. Thus, routine PTCA of the infarct-related **artery** within hours after **thrombolytic** therapy confers no benefit, and patients treated in this manner are at increased risk of...

...Two large studies have tested the hypothesis that delayed PTCA of the infarct-related **artery** after **intravenous** **thrombolytic** therapy reduces long-term morbidity and mortality. In both trials, patients receiving **intravenous** **thrombolytic** therapy were randomly assigned to undergo PTCA one to two days after infarction or to receive more conservative treatment, with PTCA performed only in the case of spontaneous or provocable **ischemia** . In the Should We Intervene Following **Thrombolysis** study, (Ref. 67) 800 patients received **intravenous** anisoylated plasminogen-streptokinase activator complex and were randomly assigned to treatment with PTCA or the ...

...similar in the two groups. In the TIMI IIB trial, (Ref. 68) 3262 patients received **intravenous** tissue plasminogen activator and were randomly assigned to undergo PTCA 18 to 48 hours later...

...in the two groups (Ref. 69). Thus, PTCA performed routinely 18 to 48 hours after **intravenous** **thrombolytic** therapy -- in the absence of spontaneous or provocable **ischemia** -- does not improve left ventricular function or survival. These studies indicate that among patients who receive **thrombolytic** therapy, PTCA should be reserved for those with symptomatic or objective evidence of **ischemia** .

...

...0 to 2 percent (Ref. 3,72,73). These events are usually caused by extensive **coronary** **arterial** dissection, intracoronary **thrombosis** , or both, with resultant vessel **occlusion** . **Coronary** **arterial** perforation, rupture, or embolization is rare (Ref. 70); the last is more likely in a saphenous- **vein** graft than in a native vessel...

...with abrupt closure, it occurs within minutes after PTCA, when they are still in the **catheterization** laboratory; in the other 25 percent, it usually occurs within 24 hours after the procedure...

...Three pathophysiologic processes may contribute to the occurrence of abrupt closure after PTCA: extensive dissection, **thrombosis** , and **coronary** vasospasm (Ref. 77,78). Some degree of intimal dissection -- characterized angiographically as a linear intraluminal...

...views. When it is extensive, however, the radiographic features are readily apparent, and the vessel **lumen** may be compromised. Extensive dissection is caused by injury of the deeper layers of the **arterial** wall, with subsequent intramural hemorrhage (Fig. 3). Ten percent of patients with **coronary** **arterial** dissection after PTCA require emergency bypass surgery, sustain a myocardial infarction, or die. In contrast...

...without extensive dissection have a serious complication (Ref. 79). *Figure 3.-Cineangiograms of the Left **Coronary** **Artery** in the Right Anterior Oblique Projection before and Immediately after PTCA of the Circumflex **Artery** . The circular wires in the right portion of each panel are sternal sutures from previous **coronary** - **artery** bypass grafting. Before **angioplasty** , a severe **stenosis** was present in the left circumflex **artery** (Panel A, arrow). When the **balloon** was **inflated** , extensive dissection occurred and propagated distally, leading to abrupt closure (Panel B, arrow) *. **FIGURE OMITTED...

...Acute **thrombus** formation after PTCA is characterized angiographically as an intraluminal filling defect or an area stained with radiographic contrast material. **Thrombus** formation is most likely to occur in patients with extensive dissection, those with a severe residual **stenosis** after

PTCA, those with preexisting intracoronary **thrombus** , and those not receiving an antiplatelet agent. In one study, 22 percent of the patients undergoing PTCA without antiplatelet therapy had **thrombi** demonstrable by angiography after dilation; in half these patients, the **thrombi** caused **occlusion** , requiring repeated PTCA, bypass surgery, or **thrombolysis** (Ref. 13). Conversely, those who received aspirin before PTCA were much less likely to have demonstrable **thrombi** afterward...

...Since most patients receive nitrates, calcium-channel blockers, or both before, during, and after PTCA, **coronary** vasospasm is an uncommon cause of abrupt closure.

Risk Factors for Abrupt Closure

Several clinical...

...abrupt closure. *Table 1. Variables Associated with an Increased Risk of Abrupt Closure of the **Artery** in Patients Undergoing PTCA *. **TABLE OMITTED**

Consequences of Abrupt Closure

The consequences of abrupt closure vary widely. Patients with adequate collateral perfusion of the **occluded** vessel may have abrupt closure without chest pain, electrocardiographic abnormalities, or hemodynamic compromise (Ref. 76). More commonly, abrupt closure is accompanied by chest discomfort and electrocardiographic evidence of **ischemia** and requires immediate revascularization of the **occluded** vessel (by means of repeated PTCA or bypass surgery) to prevent or limit myocardial injury...
...effective treatment of abrupt closure is prevention, strategies aimed at precluding its possible causes (dissection, **thrombosis** , and vasospasm) are routinely instituted. Calcium-channel blockers, nitrates, or both are usually administered before...

...patients at high risk of abrupt closure (those with angiographically demonstrable extensive dissection or intracoronary **thrombus**) are given an infusion of heparin for 12 to 24 hours after PTCA, although the...

...When abrupt closure occurs, redilation with a standard **balloon catheter** is usually attempted, which is successful in about 50 percent of patients (Ref. 75,76,85). When this strategy fails, a special **balloon catheter** known as a perfusion **catheter** may be used, if the **coronary** anatomy is suitable. Holes in the **catheter** proximal and distal to the **balloon** allow blood to flow through the **catheter** during **inflation** of the **balloon** , thus maintaining perfusion of the distal **artery** during prolonged **inflation** (10 to 30 minutes). In the majority of patients in whom a standard **balloon catheter** fails to restore sustained anterograde perfusion, a perfusion **catheter** is effective (Ref. 85,86). If these strategies are unsuccessful in restoring and stabilizing anterograde flow, further management is dictated by the amount of myocardium perfused by the **occluded artery** , the severity of symptoms or hemodynamic compromise, and the risk associated with emergency bypass surgery...

...in the ensuing days to weeks in 10 to 15 percent (Ref. 87,88). Finally, **thrombolytic** therapy (Ref. 89) or directional atherectomy (Ref. 90) has been used on occasion in patients...

...If percutaneous methods fail to restore anterograde flow in the abruptly **occluded artery** , the patient is usually referred for emergency bypass grafting. Although the early mortality associated with...

...Peripheral **vascular** complications, such as femoral **arterial** pseudoaneurysm, laceration, **arteriovenous** fistula, embolism, **arterial occlusion** , and hematoma formation, occur in about 3 percent of patients undergoing PTCA. The use of large **arterial** sheaths, the concomitant use of anticoagulant or **thrombolytic** therapy, an advanced age, and the presence of peripheral **vascular** disease increase the risk of these **vascular** complications (Ref. 93,94). Other, less common acute complications of PTCA are similar to those of diagnostic **coronary** angiography, including atrial or ventricular arrhythmias, conduction abnormalities, **coronary arterial** embolization, cardiac tamponade, allergic reactions to contrast material or one of the medications given

during...
...successful PTCA, the chief limitation to long-term, event-free survival is recurrence of the **stenosis** , or **restenosis** . Although improved medical therapy and technical advances over the past decade have reduced the incidence of abrupt closure, the incidence of **restenosis** has not changed. Several definitions of **restenosis** have been suggested, but it is most commonly defined as more than a 50 percent narrowing of the diameter of the **lumen** at the site of previously successful PTCA (Fig. 4). **Restenosis** occurs in about one third of patients in whom a narrowed **artery** has been dilated (Ref. 22,53,97,98) and in about 60 percent of those in whom a chronically **occluded artery** has been dilated (Ref. 26,27). **Restenosis** typically occurs one to three months after PTCA, and in 95 percent of patients, it occurs within six months after the procedure. **Restenosis** is uncommon less than one month or more than six months after PTCA (Ref. 12).
*Figure 4.-Cineangiograms of the Right **Coronary Artery** in the Left Anterior Oblique Projection before, during, Immediately after, and Four Months after PTCA. During the procedure, a temporary transvenous pacing **catheter** is positioned in the right ventricle (Panels A, B, and C; black arrows). The base-line angiogram shows a severe **stenosis** in the midportion of the right **coronary artery** (Panel A, white arrow). A **balloon** is positioned adjacent to the **stenosis** and is **inflated** at 8 atmospheres of pressure for 60 seconds; the extent of **inflation** is shown by the two white arrows (Panel B). The result is excellent, with no visible residual **stenosis** (Panel C, white arrow). Four months later, the patient was hospitalized with recurrent angina on exertion, and the angiogram showed evidence of **restenosis** (Panel D, arrow) *. **FIGURE OMITTED**

Mechanism of **Restenosis**

The process of **restenosis** is initiated by injury of the vessel, with the subsequent release of **thrombogenic** , vasoactive, and mitogenic factors (Ref. 99). Endothelial and deep-vessel injury leads to platelet aggregation, **thrombus** formation, inflammation, and activation of macrophages and smooth-muscle cells. These events induce the production...

...which results in the migration of smooth-muscle cells from their usual location in the **arterial** media to the intima, where they change to a synthetic phenotype, produce extracellular matrix, and proliferate, thereby resulting in a **stenosis** within the vessel **lumen** . In addition, scar contraction may occur, further reducing the size of the **lumen** (Ref. 101). These processes make up the wound-healing response that occurs in all patients...

...patients with the most pronounced reparative response to the intimal and medial damage induced by **balloon inflation** , luminal encroachment is particularly marked, and such patients are said to have **restenosis** . Contraction ...the dilated and stretched medial and adventitial layers -- so-called elastic recoil -- may contribute to **restenosis** , but such contraction is usually apparent within hours to days after PTCA (Ref. 102).

Risk Factors for **Restenosis**

Numerous clinical, anatomical, and procedural variables have been associated with an increased incidence of **restenosis** after successful PTCA (Table 2). Among the clinical variables, diabetes mellitus and unstable angina are...

...nature of these analyses, the clinical variables have limited value as a means of predicting **restenosis** in an individual patient (Ref. 106).
*Table 2. Variables Associated with an Increased Risk of **Restenosis** after PTCA *. **TABLE OMITTED**

Consequences of **Restenosis**

Most patients with **restenosis** after successful PTCA have recurrent angina, but some of those with angiographic evidence of **restenosis** are asymptomatic. Since such patients have a good prognosis, a second **angioplasty** should be reserved for those with recurrent symptoms (Ref. 118). Myocardial infarction is rarely the initial manifestation of **restenosis** . The severity of the narrowing at the site of **restenosis** is usually similar to that before PTCA (Ref. 119). However, when PTCA is performed in a minimally narrowed **coronary artery** , the **restenosis** may be more severe than the initial **stenosis** .

Management of **Restenosis**

Restenosis is often treated successfully with a second PTCA. The second procedure is more likely to...

...procedure is performed only in patients in whom the first was successful, and because the **restenosis** consists primarily of fibroproliferative tissue rather than atherosclerotic **plaque** . The incidence of **restenosis** after a second PTCA is thought to be similar to that after the initial dilation...

...Numerous pharmacologic approaches and devices have been evaluated in an attempt to prevent **restenosis** (Table 3). Fish oil, lovastatin, and trapidil (triazolopyrimidine) have shown promise in some trials, (Ref...

...pharmacologic agent may have had too few patients or used inadequate doses. The incidence of **restenosis** after elective placement of an intracoronary stent appears to be low, (Ref. 142,143) but...

...yet available. *Table 3. Pharmacologic Agents Evaluated in Randomized Trials to Reduce the Incidence of **Restenosis** after PTCA *. **TABLE OMITTED...

... **Coronary** Atherectomy

Apart from PTCA, directional **coronary** atherectomy is the only procedure approved by the Food and **Drug** **Administration** for percutaneous **coronary** revascularization that is in widespread use. With this procedure, a windowed cylindrical housing is compressed against the **stenosis** as the attached **balloon** is **inflated** against the opposite wall of the **artery** . Once the housing has been positioned, a rotating metal blade within it is advanced, which shaves **plaque** from the vessel wall and deposits the debris in the tip of the **catheter** . The luminal area is increased by the dilating effect of the device itself, **inflation** of the **balloon** , and removal of atherosclerotic material (Ref. 9,144). When atherectomy is used to treat noncalcified **stenoses** , the incidence of initial success, abrupt closure, and **restenosis** is similar to that for PTCA (Ref. 144-146...

...Two recent randomized trials compared atherectomy and PTCA. In the **Coronary** **Angioplasty** versus Excisional Atherectomy Trial (CAVEAT), the patients undergoing atherectomy had a higher incidence of angiographically documented successful revascularization but also had a higher incidence of acute complications. **Restenosis** occurred in 50 percent of the 512 patients treated with atherectomy and in 57 percent...
...likely to have a myocardial infarction within six months after the procedure. Among patients with **stenoses** of the proximal left anterior descending **artery** , atherectomy resulted in a lower incidence of **restenosis** than did PTCA (51 percent vs. 63 percent, P = 0.04), but there was no...

...The Canadian **Coronary** Atherectomy Trial compared atherectomy in 138 patients with PTCA in 136 patients, all with **stenoses** of the proximal left anterior descending **artery** . Although atherectomy resulted in a higher incidence of initially successful revascularization, the clinical outcome at...

...to the findings of CAVEAT, atherectomy and PTCA were associated with a similar incidence of **restenosis** ...and additional experience in performing it may lead to the identification of specific characteristics of **stenoses** that are more effectively approached with atherectomy...

...than bypass surgery, (Ref. 149) even though some patients who undergo PTCA require a second **angioplasty** because of **restenosis** (Ref. 150). Much of the difference in cost between PTCA and bypass surgery is attributable...
...and Quality of Life (Ref. 41) will address this question as part of the Bypass **Angioplasty** Revascularization Investigation, a randomized trial...

...more than 15 years ago, there have been notable advances in technique and equipment. Many **stenoses** -- regardless of their location, severity, or morphologic characteristics -- can now be dilated successfully. The

development...

...PTCA even further. Moreover, new antiplatelet and antithrombin agents may reduce the incidence of acute **thrombotic** complications. **Restenosis** remains a challenge; unfortunately, there has been little progress in reducing its incidence. The pathophysiology of **restenosis** is multifactorial and poorly understood. In all probability, a therapeutic approach that combines several pharmacologic and procedural innovations will be required to decrease the incidence of **restenosis** .

CITED REFERENCES

1. Dotter CT, Judkins MP. Transluminal treatment of **arteriosclerotic obstruction** : description of a new technique and a preliminary report of its application. Circulation 1964;30:654-70.
2. Gruntzig A. Transluminal dilatation of **coronary - artery stenosis** . Lancet 1978;1:263.
3. Detre K, Holubkov R, Kelsey S, et al. Percutaneous transluminal **coronary angioplasty** in 1985-1986 and 1977-1981: the National Heart, Lung, and Blood Institute Registry. N...

...1988;318:265-70.

4. Topol EJ, Ellis SG, Cosgrove DM, et al. Analysis of **coronary angioplasty** practice in the United States with an insurance-claims data base. Circulation 1993;87:1489...

...DP, Weber VJ, Haudenschild C, Gottsman SB, McGovern WA, Ryan TJ. Acute effects of transluminal **angioplasty** in three experimental models of atherosclerosis. **Arteriosclerosis** 1982;2:125-33.

6. Steele PM, Chesebro JH, Stanson AW, et al. **Balloon angioplasty** : natural history of the pathophysiological response to injury in a pig model. Circ Res 1985;57:105-12.
7. Farb A, Virmani R, Atkinson JB, Kolodgie FD. **Plaque** morphology and pathologic changes in **arteries** from patients dying after **coronary balloon angioplasty** . J Am Coll Cardiol 1990;16:1421-9.
8. Soward AL, Essed CE, Serruys PW. **Coronary arterial** findings after accidental death immediately after successful percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1985;56:794-5.
9. Tenaglia AN, Buller CE, Kisslo KB, Stack RS, Davidson CJ. Mechanisms of **balloon angioplasty** and directional **coronary** atherectomy as assessed by intracoronary ultrasound. J Am Coll Cardiol 1992;20:685-91.

10. Potkin BN, Keren G, Mintz GS, et al. **Arterial** responses to **balloon coronary angioplasty** : an **intravascular** ultrasound study. J Am Coll Cardiol 1992;20:942-51.
11. Waller BF. Early and late morphologic changes in human **coronary arteries** after percutaneous transluminal **coronary angioplasty** . Clin Cardiol 1983;6:363-72.
12. Nobuyoshi M, Kimura T, Nosaka H, et al. **Restenosis** after successful percutaneous transluminal **coronary angioplasty** : serial angiographic follow-up of 229 patients. J Am Coll Cardiol 1988;12:616-23...

...ES, Schwartz JS, Taylor L, et al. Aspirin and dipyridamole in the prevention of acute **coronary thrombosis** complicating **coronary angioplasty** . Circulation 1987;76:125-34.

14. Schwartz L, Bourassa MG, Lesperance J, et al. Aspirin and dipyridamole in the prevention of **restenosis** after percutaneous transluminal **coronary angioplasty** . N Engl J Med 1988;318:1714-9.
15. Lembo NJ, Black AJR, Roubin GS...

...aspirin versus aspirin plus dipyridamole on frequency and type of acute complications of percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1990;65:422-6.

16. Bertrand ME, Allain H, Lablanche JM, TACT...

...Results of a randomized trial of ticlopidine versus placebo for prevention of acute closure and **restenosis** after **coronary angioplasty** (PTCA): the TACT study. Circulation 1990;82:Suppl III:III-190. abstract.

17. McGarry TF...

...Morganroth J, et al. The relationship of anticoagulation level and complications after successful percutaneous transluminal **coronary angioplasty** . Am Heart J 1992;123:1445-51.
18. Gabliani G, Deligonul U, Kern MJ, Vandormael M. Acute **coronary occlusion** occurring after successful percutaneous transluminal **coronary angioplasty** : temporal relationship to discontinuation of anticoagulation. Am Heart J 1988;116:696-700.
19. Fischell TA, Derby G, Tse TM, Stadius ML. **Coronary artery** vasoconstriction routinely occurs after percutaneous transluminal **coronary angioplasty** : a quantitative **arteriographic** analysis. Circulation 1988;78:1323-34.
20. Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal **coronary angioplasty** : a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal **Coronary Angioplasty**). J Am Coll Cardiol 1988;12:529-45.
21. Popma JJ, Dehmer GJ. Care of the patient after **coronary angioplasty** . Ann Intern Med 1989;110:547-59.
22. Gruentzig AR, King SB III, Schlumpf M, Siegenthaler W. Long-term follow-up after percutaneous transluminal **coronary angioplasty** : the early Zurich experience. N Engl J Med 1987;316:1127-32.
23. Hollman J, Simpfendorfer C, Franco I, Whitlow P, Goormastic M. Multivessel and single-vessel **coronary angioplasty** : a comparative study. Am Heart J 1992;124:9-12.
24. Parisi AF, Folland ED, Hartigan P. A comparison of **angioplasty** with medical therapy in the treatment of single-vessel **coronary artery** disease. N Engl J Med 1992;326:10-6.
25. Ellis SG. Elective **coronary angioplasty** : technique and complications. In: Topol EJ, ed. Textbook of interventional cardiology. Philadelphia: W.B. Saunders, 1990:200-1.
26. Meier B. Total **coronary occlusion** : a different animal? J Am Coll Cardiol 1991;17:Suppl B:50B-57B.
27. Bell...
...GS, Bailey KR, Holmes DR Jr. Initial and long-term outcome of 354 patients after **coronary balloon angioplasty** of total **coronary artery occlusions** . Circulation 1992;85:1003-11.
28. Ivanhoe RJ, Weintraub WS, Douglas JS Jr, et al. Percutaneous transluminal **coronary angioplasty** of chronic total **occlusions** : primary success, **restenosis** , and long-term clinical follow-up. Circulation 1992;85:106-15.
29. Stone GW, Rutherford BD, McConahay DR, et al. Procedural outcome of **angioplasty** for total **coronary artery occlusion** : an analysis of 971 lesions in 905 patients. J Am Coll Cardiol 1990;15:849...

...Ruocco NA Jr, Ring ME, Holubkov R, Jacobs AK, Detre KM, Faxon DP. Results of **coronary angioplasty** of chronic total **occlusions** (the National Heart, Lung, and Blood Institute 1985-1986 Percutaneous Transluminal **Angioplasty** Registry). Am J Cardiol 1992;69:69-76.
31. Killip T. Twenty years of **coronary** bypass surgery. N Engl J Med 1988;319:366-8.
32. Webb JG, Myler RK, Shaw RE, et al. **Coronary angioplasty** after **coronary** bypass surgery: initial results and late outcome in 422 patients. J Am Coll Cardiol 1990;16:812-20.
33. Platko WP, Hollman J, Whitlow PL, Franco I. Percutaneous transluminal **angioplasty** of saphenous **vein** graft **stenosis** : long-term follow-up. J Am Coll Cardiol 1989;14:1645-50.
34. de Feyter PJ, van Suylen R-J, de Jaegere PPT, Topol EJ, Serruys PW. **Balloon angioplasty** for the treatment of lesions in saphenous **vein** bypass grafts. J Am Coll Cardiol 1993;21:1539-49.
35. Urban P, Sigwart U, Golf S, Kaufmann U, Sadeghi H, Kappenberger L. **Intravascular** stenting for **stenosis** of aortocoronary **venous** bypass grafts. J Am Coll Cardiol 1989;13:1085-91.
36. Faxon DP, Ruocco N, Jacobs AK. Long-term outcome of patients after percutaneous transluminal **coronary angioplasty** . Circulation 1990;81: Suppl IV:IV-9-IV-13.

37. Bourassa MG, Holubkov R, Yeh W, Detre KM, Co-investigators of the National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. Strategy of complete revascularization in patients with multivessel **coronary artery** disease (a report from the 1985-1986 NHLBI PTCA Registry). Am J Cardiol 1992;70:174-8.
38. Wohlgelernter D, Cleman M, Highman HA, Zaret BL. Percutaneous transluminal **coronary angioplasty** of the ``culprit lesion'' for management of unstable angina pectoris in patients with multivessel **coronary artery** disease. Am J Cardiol 1986;58:460-4.
39. King SB III, Lembo NJ, Hall EC, EAST Investigators. The Emory **Angioplasty** vs. Surgery Trial (EAST): analysis of baseline patient characteristics. Circulation 1990;82:Suppl III:III...

...Balino N, Paviotti C, Sosa Liprandi MI, Palacios IF. Argentine randomized trial of percutaneous transluminal **coronary angioplasty** versus **coronary artery** bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. J Am Coll Cardiol 1993;22:1060-7.
41. Landau C, Faxon DP. Acronyms in **angioplasty** and **restenosis** : a summary of recent and ongoing clinical randomized trials. J Interv Cardiol 1992;5:29-37.
42. RITA Trial Participants. **Coronary angioplasty** versus **coronary artery** bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. Lancet 1993;341:573-80.
43. Leeman DE, McCabe CH, Faxon DP, et al. Use of percutaneous transluminal **coronary angioplasty** and bypass surgery despite improved medical therapy for unstable angina pectoris. Am J Cardiol 1988...

...577-81.
47. de Feyter PJ, Serruys PW, van den Brand M, et al. Emergency **coronary angioplasty** in refractory unstable angina. N Engl J Med 1985;313:342-6.
48. Stammen F, De Scheerder I, Glazier JJ, et al. Immediate and follow-up results of the conservative **coronary angioplasty** strategy for unstable angina pectoris. Am J Cardiol 1992;69:1533-7.
49. Myler RK, Shaw RE, Stertzer SH, et al. Unstable angina and **coronary angioplasty** . Circulation 1990;82:Suppl II:II-88-II-95.
50. de Feyter PJ, Serruys PW, v d Brand M, Hugenholtz PG. Percutaneous transluminal **coronary angioplasty** for unstable angina. Am J Cardiol 1991;68:Suppl:125B-135B.
51. Holmes DR Jr, Holubkov R, Vlietstra RE, et al. Comparison of complications during percutaneous transluminal **coronary angioplasty** from 1977 to 1981 and from 1985 to 1986: the National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. J Am Coll Cardiol 1988;12:1149-55.
52. Lambert M, Bonan R, Cote G, et al. Multiple **coronary angioplasty** : a model to discriminate systemic and procedural factors related to **restenosis** . J Am Coll Cardiol 1988;12:310-4.
53. Leimgruber PP, Roubin GS, Hollman J, et al. **Restenosis** after successful **coronary angioplasty** in patients with single-vessel disease. Circulation 1986;73:710-7.
54. Laskey MAL, Deutsch E, Barnathan E, Laskey WK. Influence of heparin therapy on percutaneous transluminal **coronary angioplasty** outcome in unstable angina pectoris. Am J Cardiol 1990;65:1425-9.
55. Perry RA, Seth A, Hunt A, Shiu MF. **Coronary angioplasty** in unstable angina and stable angina: a comparison of success and complications. Br Heart J 1988;60:367-72.
56. Ambrose JA, Torre SR, Sharma SK, et al. Adjunctive **thrombolytic** therapy for **angioplasty** in **ischemic** rest angina: results of a double-blind randomized pilot study. J Am Coll Cardiol 1992...

...1197-204.
57. Grines CL, Browne KF, Marco J, et al. A comparison of immediate **angioplasty** with **thrombolytic** therapy for acute myocardial infarction. N Engl J Med 1993;328:673-9.
58. Zijlstra...

...de Boer MJ, Hoorntje JCA, Reiffers S, Reiber JHC, Suryapranata H. A comparison of immediate **coronary angioplasty** with **intravenous** streptokinase in acute myocardial infarction. N Engl J Med 1993;328:680-4.
59. Gibbons RJ, Holmes DR, Reeder GS, et al. Immediate **angioplasty** compared with the **administration** of a **thrombolytic** agent followed by conservative treatment for myocardial infarction. N Engl J Med 1993;328:685-91.
60. Landau C, Glamann DB, Willard JE, Hillis LD, Lange RA. **Coronary angioplasty** in the patient with acute myocardial infarction. Am J Med (in press).
61. Neuhaus KL, Von Essen R, Tebbe U, et al. Improved **thrombolysis** in acute myocardial infarction with front-loaded **administration** of alteplase: results of the rt-PA-APSAC patency study (TAPS). J Am Coll Cardiol...

...EJ, Califf RM, George BS, et al. A randomized trial of immediate versus delayed elective **angioplasty** after **intravenous** tissue plasminogen activator in acute myocardial infarction. N Engl J Med 1987;317:581-8.
63. TIMI Research Group. Immediate vs delayed **catheterization** and **angioplasty** following **thrombolytic** therapy for acute myocardial infarction: TIMI II A results. JAMA 1988;260:2849-58.
64. Simoons ML, Arnold AER, Betriu A, et al. **Thrombolysis** with tissue plasminogen activator in acute myocardial infarction: no additional benefit from immediate percutaneous **coronary angioplasty** . Lancet 1988;1:197-203.
65. Arnold AER, Simoons ML, Van de Werf F, et al. Recombinant tissue-type plasminogen activator and immediate **angioplasty** in acute myocardial infarction: one-year follow-up. Circulation 1992;86:111-20.
66. O'Neill WW, Weintraub R, Grines CL, et al. A prospective, placebo-controlled, randomized trial of **intravenous** streptokinase and **angioplasty** versus lone **angioplasty** therapy of acute myocardial infarction. Circulation 1992;86:1710-7.
67. SWIFT (Should We Intervene Following **Thrombolysis** ?) Trial Study Group. SWIFT trial of delayed elective intervention v conservative treatment after **thrombolysis** with anistreplase in acute myocardial infarction. BMJ 1991;302:555-60.
68. TIMI Study Group. Comparison of invasive and conservative strategies after treatment with **intravenous** tissue plasminogen activator in acute myocardial infarction: results of the **Thrombolysis** in Myocardial Infarction (TIMI) phase II trial. N Engl J Med 1989;320:618-27.
69. Williams DO, Braunwald E, Knatterud G, et al. One-year results of the **Thrombolysis** in Myocardial Infarction Investigation (TIMI) phase II trial. Circulation 1992;85:533-42.
70. Cowley MJ, Dorros G, Kelsey SF, Van Raden M, Detre KM. Acute **coronary** events associated with percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1984;53:12C-16C.
71. Talley JD, Weintraub WS, Roubin GS, et al. Failed elective percutaneous transluminal **coronary angioplasty** requiring **coronary artery** bypass surgery: in-hospital and late clinical outcome at 5 years. Circulation 1990;82:1203-13.
72. Hartz AJ, Kuhn EM, Pryor DB, et al. Mortality after **coronary angioplasty** and **coronary artery** bypass surgery (the national Medicare experience). Am J Cardiol 1992;70:179-85.
73. Myler RK, Shaw RE, Stertzer SH, et al. Lesion morphology and **coronary angioplasty** : current experience and analysis. J Am Coll Cardiol 1992;19:1641-52.
74. Ellis SG...

...King SB III, et al. Angiographic and clinical predictors of acute closure after native vessel **coronary angioplasty** . Circulation 1988;77:372-9.
75. Simpfendorfer C, Balardi J, Bellamy G, Galan K, Franco I, Hollman J. Frequency, management and follow-up of patients with acute **coronary occlusions** after percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1987;59:267-9.
76. Sinclair IN, McCabe CH, Sipperly ME, Baim...

...77. Lincoff AM, Popma JJ, Ellis SG, Hacker JA, Topol EJ. Abrupt vessel closure complicating **coronary angioplasty** : clinical, angiographic and therapeutic profile. J Am Coll Cardiol 1992;19:926-35.
78. Mabin TA, Holmes DR Jr, Smith HC, et al. Intracoronary **thrombus** : role in **coronary occlusion** complicating percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1985;5:198-202.
79. Bredlau CE, Roubin GS, Leimgruber PP...
...Jr, King SB III, Gruentzig AR. In-hospital morbidity and mortality in patients undergoing elective **coronary angioplasty** . Circulation 1985;72:1044-52.
80. Detre KM, Holmes DR Jr, Holubkov R, et al. Incidence and consequences of periprocedural **occlusion** : the 1985-1986 National Heart, Lung, and Blood Institute Percutaneous Transluminal **Coronary Angioplasty** Registry. Circulation 1990;82:739-50.
81. de Feyter PJ, van den Brand M, Laarman GJ, et al. Acute **coronary artery occlusion** during and after percutaneous transluminal **coronary angioplasty** : frequency, prediction, clinical course, management, and follow-up. Circulation 1991;83:927-36.
82. Ellis SG, Topol EJ. Results of percutaneous transluminal **coronary angioplasty** of high-risk angulated **stenoses** . Am J Cardiol 1990;66:932-7.
83. Savage MP, Goldberg S, Hirshfeld JW, et al. Clinical and angiographic determinants of primary **coronary angioplasty** success. J Am Coll Cardiol 1991;17:22-8.
84. Roubin GS, Douglas JS Jr, King SB III, et al. Influence of **balloon** size on initial success, acute complications, and **restenosis** after percutaneous transluminal **coronary angioplasty** : a prospective randomized study. Circulation 1988;78:557-65.
85. Leitschuh ML, Mills RM Jr, Jacobs AK, Ruocco NA Jr, LaRosa D, Faxon DP. Outcome after major dissection during **coronary angioplasty** using the perfusion **balloon catheter** . Am J Cardiol 1991;67:1056-60.
86. Van Lierde JM, Glazier JJ, Stammen FJ, et al. Use of an autoperfusion **catheter** in the treatment of acute refractory vessel closure after **coronary balloon angioplasty** : immediate and six month follow up results. Br Heart J 1992;68:51-4.
87...

...AD, Agrawal SK, et al. Intracoronary stenting for acute and threatened closure complicating percutaneous transluminal **coronary angioplasty** . Circulation 1992;85:916-27.
88. Lincoff AM, Topol EJ, Chapekis AT, et al. Intracoronary stenting compared with conventional therapy for abrupt vessel closure complicating **coronary angioplasty** : a matched case-control study. J Am Coll Cardiol 1993;21:866-75.
89. Schieman G, Cohen BM, Kozina J, et al. Intracoronary urokinase for intracoronary **thrombus** accumulation complicating percutaneous transluminal **coronary angioplasty** in acute **ischemic** syndromes. Circulation 1990;82:2052-60.
90. Lee TC, Hartzler GO, Rutherford BD, McConahay DR. Removal of an **occlusive coronary** dissection flap by using an atherectomy **catheter** . Cathet Cardiovasc Diagn 1990;20:185-8.
91. Lazar HL, Faxon DP, Paone G, et al. Changing profiles of failed **coronary angioplasty** patients: impact on surgical results. Ann Thorac Surg 1992;53:269-73.
92. Landau C...

...Suppl II:II-291. abstract.
93. Muller DWM, Shamir KJ, Ellis SG, Topol EJ. Peripheral **vascular** complications after conventional and complex percutaneous **coronary** interventional procedures. Am J Cardiol 1992;69:63-8.
94. Oweida SW, Roubin GS, Smith RB III, Salam AA. Postcatheterization **vascular** complications associated with percutaneous transluminal **coronary angioplasty** . J Vasc Surg 1990;12:310-5.
95. Wyman RM, Safian RD, Portway V, Skillman JJ, McKay RG, Baim DS. Current complications of diagnostic and therapeutic cardiac **catheterization** . J Am Coll Cardiol 1988;12:1400-6.
96. Landau C, Lange RA, Glamann DB, Willard JE, Hillis LD. Vasovagal

reactions in the cardiac **catheterization** laboratory. Am J Cardiol 1994;73:95-7.
97. MERCATOR Study Group. Does the new angiotensin converting enzyme inhibitor cilazapril prevent **restenosis** after percutaneous transluminal **coronary angioplasty** ? Results of the MERCATOR study: a multicenter, randomized, double-blind placebo-controlled trial. Circulation 1992;86:100-10.
98. Hirshfeld JW Jr, Schwartz JS, Jugo R, et al. **Restenosis** after **coronary angioplasty** : a multivariate statistical model to relate lesion and procedure variables to **restenosis** . J Am Coll Cardiol 1991;18:647-56.
99. Lange RA, Willard JE, Hillis LD. **Restenosis** : the Achilles heel of **coronary angioplasty** . Am J Med Sci 1993;306:265-75.
100. Libby P, Schwartz D, Brogi E, Tanaka H, Clinton SK. A cascade model for **restenosis** : a special case of atherosclerosis progression. Circulation 1992;86:Suppl III:III-47-III-52.
101. Haudenschild **CC** . Pathobiology of **restenosis** after **angioplasty** . Am J Med 1993;94:Suppl 4A:4A-40S-4A-44S.
102. Haude M, Erbel R, Issa H, Meyer J. Quantitative analysis of elastic recoil after **balloon angioplasty** and after intracoronary implantation of **balloon** -expandable Palmaz-Schatz stents. J Am Coll Cardiol 1993;21:26-34.
103. Holmes DR Jr, Vlietstra RE, Smith HC, et al. **Restenosis** after percutaneous transluminal **coronary angioplasty** (PTCA): a report from the PTCA Registry of the National Heart, Lung, and Blood Institute ...

...81C.
104. Galan KM, Deligonul U, Kern MJ, Chaitman BR, Vandormael MG. Increased frequency of **restenosis** in patients continuing to smoke cigarettes after percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1988;61:260-3.
105. Austin GE, Lynn M, Hollman J. Laboratory test results as predictors of recurrent **coronary artery stenosis** following **angioplasty** . Arch Pathol Lab Med 1987;111:1158-62.
106. Weintraub WS, Kosinski AS, Brown CL III, King SB III. Can **restenosis** after **coronary angioplasty** be predicted from clinical variables? J Am Coll Cardiol 1993;21:6-14.
107. Reis GJ, Kuntz RE, Silverman DI, Pasternak RC. Effects of serum lipid levels on **restenosis** after **coronary angioplasty** . Am J Cardiol 1991;68:1431-5.
108. Kahn JK, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Hartzler GO. Short- and long-term outcome of percutaneous transluminal **coronary angioplasty** in chronic dialysis patients. Am Heart J 1990;119:484-9.

109. Guiteras Val P, Bourassa MG, David PR, et al. **Restenosis** after successful percutaneous transluminal **coronary angioplasty** : the Montreal Heart Institute experience. Am J Cardiol 1987;60:Suppl:50B-55B.
110. Leisch...
...Kerschner K, Herbinger W. Influence of a variant angina on the results of percutaneous transluminal **coronary angioplasty** . Br Heart J 1986;56:341-5.
111. Black AJR, Anderson HV, Roubin GS, Powelson SW, Douglas JS Jr, King SB III. Repeat **coronary angioplasty** : correlates of a second **restenosis** . J Am Coll Cardiol 1988;11:714-8.
112. Quigley PJ, Hlatky MA, Hinohara T, et al. Repeat percutaneous transluminal **coronary angioplasty** and predictors of recurrent **restenosis** . Am J Cardiol 1989;63:409-13.
113. Vandormael MG, Deligonul U, Kern MJ, et al. Multilesion **coronary angioplasty** : clinical and angiographic follow-up. J Am Coll Cardiol 1987;10:246-52.
114. Roubin GS, King SB III, Douglas JS Jr. **Restenosis** after percutaneous transluminal **coronary angioplasty** : the Emory University Hospital experience. Am J Cardiol 1987;60:Suppl:39B-43B.
115. Bourassa MG, Lesperance J, Eastwood C, et al. Clinical, physiologic, anatomic and procedural factors predictive of **restenosis** after percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol

1991;18:368-76.
116. Kuntz RE, Gibson CM, Nobuyoshi M, Baim DS. Generalized model of **restenosis** after conventional **balloon angioplasty** , stenting and directional atherectomy. J Am Coll Cardiol 1993;21:15-25.
117. Nichols AB, Smith R, Berke AD, Shlofmitz RA, Powers ER. Importance of **balloon** size in **coronary angioplasty** . J Am Coll Cardiol 1989;13:1094-100.
118. Hernandez RA, Macaya C, Iniguez A, et al. Midterm outcome of patients with asymptomatic **restenosis** after **coronary balloon angioplasty** . J Am Coll Cardiol 1992;19:1402-9.
119. Foley DP, Hermans WR, Rutsch W, et al. **Restenosis** after PTCA affects the entire vessel segment dilated. J Am Coll Cardiol 1993;21:Suppl A: 322A. abstract.
120. Chesebro JH, Webster MW, Reeder GS, et al. **Coronary angioplasty** : antiplatelet therapy reduces acute complications but not **restenosis** . Circulation 1989;80:Suppl II:II-64. abstract.
121. Knudtson ML, Flintoft VF, Roth DL, Hansen JL, Duff HJ. Effect of short-term prostacyclin administration on **restenosis** after percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1990;15:691-7.
122. Raizner A, Hollman J, Demke D...

...II:II-290. abstract.
123. Serruys PW, Rutsch W, Heyndrickx GR, et al. Prevention of **restenosis** after percutaneous transluminal **coronary angioplasty** with **thromboxane** A2-receptor blockade: a randomized, double-blind, placebo-controlled trial: **Coronary Artery Restenosis** Prevention on Repeated **Thromboxane** -Antagonism Study (CARPORT). Circulation 1991;84:1568-80.
124. Klein W, Eber B, Dusleag J, et al. Ketanserin prevents early **restenosis** following percutaneous transluminal **coronary angioplasty** . Clin Physiol Biochem 1990;8:Suppl 3:101-7.
125. Serruys PW, Klein W, Rutsch W, et al. PARK: the Post **Angioplasty Restenosis** Ketanserin trial. J Am Coll Cardiol 1993;21:Suppl A:322A. abstract.
126. Ellis SG...

...Jr, King SB III. Effect of 18- to 24-hour heparin administration for prevention of **restenosis** after uncomplicated **coronary angioplasty** . Am Heart J 1989;117:777-82.
127. Thornton MA, Gruentzig AR, Hollman J, King SB III, Douglas JS. Coumadin and aspirin in prevention of recurrence after transluminal **coronary angioplasty** : a randomized study. Circulation 1984;69:721-7.

128. Urban P, Buller N, Fox K, Shapiro L, Bayliss J, Rickards A. Lack of effect of warfarin on the **restenosis** rate or on clinical outcome after **balloon coronary angioplasty** . Br Heart J 1988;60:485-8.
129. Whitworth HB, Roubin GS, Hollman J, et al. Effect of nifedipine on recurrent **stenosis** after percutaneous transluminal **coronary angioplasty** . J Am Coll Cardiol 1986;8:1271-6.
130. O'Keefe JH Jr, Giorgi LV, Hartzler GO, et al. Effects of diltiazem on complications and **restenosis** after **coronary angioplasty** . Am J Cardiol 1991;67:373-6.
131. Corcos T, David PR, Val PG, et al. Failure of diltiazem to prevent **restenosis** after percutaneous transluminal **coronary angioplasty** . Am Heart J 1985;109:926-31.
132. Pepine CJ, Hirshfeld JW, Macdonald RG, et al. A controlled trial of corticosteroids to prevent **restenosis** after **coronary angioplasty** : M-HEART Group. Circulation 1990;81:1753-61.
133. O'Keefe JH Jr, McCallister BD, Bateman TM, Kuhnlein DL, Ligon RW, Hartzler GO. Ineffectiveness of colchicine for the prevention of **restenosis** after **coronary angioplasty** . J Am Coll Cardiol 1992;19:1597-600.
134. Dehmer GJ, Popma JJ, van den Berg EK, et al. Reduction in the rate of early **restenosis** after **coronary angioplasty** by a diet supplemented with n-3 fatty acids. N Engl J Med 1988;319...

...RA, Leffingwell A, et al. Usefulness of fish oil supplements in

preventing clinical evidence of **restenosis** after percutaneous transluminal **coronary angioplasty** . Am J Cardiol 1989;64:294-9.
136. Reis GJ, Boucher TM, Sipperly ME, et al. Randomised trial of fish oil for prevention of **restenosis** after **coronary angioplasty** . Lancet 1989;2:177-81.
137. Grigg LE, Kay TWH, Valentine PA, et al. Determinants of **restenosis** and lack of effect of dietary supplementation with eicosapentaenoic acid on the incidence of **coronary artery restenosis** after **angioplasty** . J Am Coll Cardiol 1989;13:665-72.
138. Bairati I, Roy L, Meyer F. Double-blind, randomized, controlled trial of fish oil supplements in prevention of recurrence of **stenosis** after **coronary angioplasty** . Circulation 1992;85:950-6.
139. Sahni R, Maniet AR, Voci G, Banka VS. Prevention of **restenosis** by lovastatin after successful **coronary angioplasty** . Am Heart J 1991;121:1600-8.
140. Hollman J, Konrad K, Raymond R, Whitlow P, Michalak M, Van Lente F. Lipid lowering for the prevention of recurrent **stenosis** following **coronary angioplasty** . Circulation 1989;80:Suppl II:II-65. abstract.
141. Okamoto S, Inden M, Setsuda M...

...T, Nakano T. Effects of trapidil (triazolopyrimidine), a platelet-derived growth factor antagonist, in preventing **restenosis** after percutaneous transluminal **coronary angioplasty** . Am Heart J 1992;123:1439-44.
142. Serruys PW, Strauss BH, Beatt KJ, et al. Angiographic follow-up after placement of a self-expanding **coronary - artery** stent. N Engl J Med 1991;324:13-7.
143. Kimura T, Nosaka H, Yokoi...

...M, Nobuyoshi M. Serial angiographic follow-up after Palmaz-Schatz stent implantation: comparison with conventional **balloon angioplasty** . J Am Coll Cardiol 1993;21:1557-63.
144. Safian RD, Gelbfish JS, Erny RE, Schnitt SJ, Schmidt DA, Baim DS. **Coronary** atherectomy: clinical, angiographic, and histological findings and observations regarding potential mechanisms. Circulation 1990;82:69-79.
145. Hillis LD. Efficacy and safety of **coronary balloon angioplasty** and directional atherectomy. Circulation 1990;82:305-7.
146. Popma JJ, Topol EJ, Hinohara T, et al. Abrupt vessel closure after directional **coronary** atherectomy. J Am Coll Cardiol 1992;19:1372-9.
147. Topol EJ, Leya F, Pinkerton CA, et al. A comparison of directional atherectomy with **coronary angioplasty** in patients with **coronary artery** disease. N Engl J Med 1993;329:221-7.
148. Adelman AG, Cohen EA, Kimball BP, et al. A comparison of directional atherectomy with **balloon angioplasty** for lesions of the left anterior descending **coronary artery** . N Engl J Med 1993;329:228-33.
149. Cohen DJ, Breall JA, Ho KKL, et al. Economics of elective **coronary** revascularization: comparison of costs and charges for conventional **angioplasty** , directional atherectomy, stenting and bypass surgery. J Am Coll Cardiol 1993;22:1052-9.
150. Black AJR, Roubin GS, Sutor C, et al. Comparative costs of percutaneous transluminal **coronary angioplasty** and **coronary artery** bypass grafting in multivessel **coronary artery** disease. Am J Cardiol 1988;62:809-11. □ ...

```
Set     Items   Description
S1     175992   (VENOUS OR VEIN? OR ARTERY OR ARTERI? OR VASCULAR? OR INTR-
             ?VASC? OR INTR?VEN? OR BLOOD?()VESSEL? OR VENAL OR CORONAR?)
S2      78229   OCCLUD? OR OCCLUSI? OR OBSTRUCT? OR STENOS? OR STENOT? OR -
             RESTENOS? OR RESTENOT? OR PLAQUE?
S3      66259   SCLERO? OR THROMB? OR BLOODCLOT? OR BLOOD()CLOT? OR ISCHEM-
             I? OR ARTER?SCLER? OR PLAQUING
S4        367   CALCIUM()DEPOSIT?
S5     340080   BALLOON? OR PLASTY? OR PLASTIE? ? OR ANGIOPLAST? OR OCCLU?-
             ()DEVICE? OR INFLAT? OR CARDIOPLAST?
S6          1   ARTERIOPLAST?
S7    4824648   DELIVER? OR ADMINIST? OR INJECT? OR INFUS? OR PERFUS?
S8      43377   CATHETER? OR CANNULA? OR CANULA? OR TROCAR? OR LUMEN? OR H-
             OLLOW?(N)WIRE?
S9    1199591   DRUG? OR NARCOTIC? OR OCCLU?(N)TREAT? OR ANTICOAGUL? OR AN-
             TI()COAGUL? OR THROMBYT?
S10     8178   RADIONUCLID? OR RADIO()NUCLID? OR RADIOISOTOP? OR RADIO()I-
             SOTOP? OR RADIOACTIVE()ISOTOP?
S11        6   RADIO()ACTIVE()ISOTOP?
S12    95165   FLOWRATE? OR FLOW()RATE? OR "CC" OR "C.C." OR CUBIC()CENTI-
             L?
S13   238441   S7(10N)(S9 OR S10 OR S11)
S14      214   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6) AND S8 AND S12
S15       71   S13 AND S14
S16    75218   S3 OR ARTERI?SCLER? OR ARTER?()SCLER? OR ARTHER?SCLER? OR -
             ARTHER?()SCLER? OR ATHER?SCLER? OR ATHER?()SCLER?
S17   340117   S5 OR (CARDIO? OR ANGIO?)()PLAST?
S18  1200917   S9 OR THROMBOL?
S19    95709   S12 OR (INFUS? OR PERFUS?)()RATE?
S20   238893   S7(10N)(S9 OR S10 OR S11 OR S18)
S21      242   S1 AND (S2 OR S3 OR S4) AND (S5 OR S6 OR S17) AND S8 AND (-
             S12 OR S19)
S22       99   S20 AND S21
S23    25838   S1(10N)(S2 OR S3 OR S4)
S24   340118   S5 OR S6 OR S17
S25   238893   S7(10N)(S9 OR S10 OR S11 OR S18)
S26      164   S8(10N)(S12 OR S19)
S27        4   S23 AND S24 AND S25 AND S26
S28        2   S27 AND PY<1999
S29    22480   1(S)(S2 OR S3 OR S4)
S30    22107   29 AND S25
S31    52617   7(S)(S9 OR S10 OR S11 OR S18)
S32    20121   30 AND S31
S33      965   S9(S)(S12 OR S19)
S34     2979   S29 AND S31
S35      235   S31 AND S33
S36   718134   35 AND PY<1999
S37      193   S35 AND PY<1999
S38      118   S37 AND S20
?show files
File  16:Gale Group PROMT(R) 1990-2003/Sep 26
         (c) 2003 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2003/Sep 29
         (c)2003 The Gale Group
File 621:Gale Group New Prod.Annou.(R) 1985-2003/Sep 29
         (c) 2003 The Gale Group
File 444:New England Journal of Med. 1985-2003/Sep W4
         (c) 2003 Mass. Med. Soc.
?
```

38/5,K/18 (Item 8 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

09082591 SUPPLIER NUMBER: 18802892 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Pharmaceuticals in the new millennium. (Chemical Market Reporter: 125 Years)
Gerry, Roberta
Chemical Marketing Reporter, v250, n17, pS80(7)
Oct 21, 1996
ISSN: 0090-0907 LANGUAGE: English RECORD TYPE: Fulltext; Abstract
WORD COUNT: 2234 LINE COUNT: 00182

ABSTRACT: The pharmaceutical industry is undergoing a period of deep-seated, revolutionary change as the new millenium approaches. The imperatives of competition and of developing new products to treat diseases which did not exist at the turn of the century is driving a wave of mega-acquisitions throughout the industry. The structure of the industry is also changing as pharmaceutical companies merge with chemical companies and assume an increasingly globalized and integrated character.

SPECIAL FEATURES: illustration; photograph
INDUSTRY CODES/NAMES: CHEM Chemicals, Plastics and Rubber; BUSN Any type of business
DESCRIPTORS: Pharmaceutical industry--Management
PRODUCT/INDUSTRY NAMES: 2834000 (Pharmaceutical Preparations)
SIC CODES: 2834 Pharmaceutical preparations
FILE SEGMENT: TI File 148

... interstate commerce and required "honest labeling."
In 1928, Congress authorized the organization of the Food, **Drug** & Insecticide **Administration** as a separate unit to engage in research and technical work associated with the execution...

...And, in 1938, the agency's jurisdiction was expanded with the passage of the Food, **Drug** & Cosmetic Act.
From the very onset, Food & **Drug** **Administration** has been agonizingly slow in approving new **drugs** . However, in the last four years, the pace has quickened noticeably. As recently as 1987...

...has been running a direct-to-consumers advertising campaign urging patients who take a rival **drug** , Pfizer's Procardia XL, to ask their doctors to switch them to Adalat **CC** for a 28 percent savings.
On the sensitive issue of drug prices, the public perception...of pharmaceutica)s and biotechnology, it is predicted, will produce a whole new generation of **drugs** . In 1993, SmithKline Beecham made a $125 million deal for 7 percent of Human Genome Sciences of Rockville, MD, which gave SmithKline access to the largest...

19961021

38/5,K/50 (Item 40 from file: 148)
DIALOG(R)File 148:Gale Group Trade & Industry DB

06517844 SUPPLIER NUMBER: 13594395 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Dissolution and bioavailability of drug delivery **systems. (parameters evaluated affecting performance of** drug delivery **systems with comparison of in vitro and in vivo measurements)**
Banakar, Umesh V.
Manufacturing Chemist, v64, n1, p18(5)
Jan, 1993
ISSN: 0262-4230 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT
WORD COUNT: 3526 LINE COUNT: 00297

SPECIAL FEATURES: illustration; table; graph
INDUSTRY CODES/NAMES: CHEM Chemicals, Plastics and Rubber; ENG Engineering and Manufacturing; INTL Business, International

DESCRIPTORS: **Drug delivery** systems--Evaluation; Bioavailability--Measurement; Solution (Chemistry)--Analysis
FILE SEGMENT: TI File 148

Dissolution and bioavailability of drug delivery **systems. (parameters evaluated affecting performance of** drug delivery **systems with comparison of in vitro and in vivo measurements)**
... activity of the intestinal microflora, and dissolution rate.
The slowest of rate-limiting steps in **drug** absorption are blood flow (**perfusion rate** -limited), or **drug** penetration through the membrane diffusion rate-limited). With highly lipid-soluble **drugs** or those that are able to pass freely through aqueous filled pores, penetration through a membrane may be so rapid that equilibrium is promptly established between the **drug** concentration at the absorption site and that of **drug** in blood. Under these conditions the rate-limiting step controlling **drug** absorption is blood flow.
Figure 2 exemplifies this phenomenon. Tritiated water moves freely through aqueous...

...and then its absorption is insensitive to changes in blood flow.
In general, absorption of **drugs** in solution from muscle and subcutaneous tissue is **perfusion rate** -limited. Increased blood flow increases absorption. The main barrier to **drug** absorption here is the capillary wall, which at these sites is much more loosely knit...

...prolonged gastrointestinal residence time (Fig. 4). The presence of larger fluid volume coupled with rapid **drug delivery** to an environment that is more suitable for absorption will provide better and more reproducible...
...the gut wall may be inhibited or induced by dietary, or environmental xenobiotics, and co- **administered drugs** . Phase 1 and Phase 2 metabolic reactions occurring in the gut wall of humans is...

...by organisms residing in the lower gut and hence has minimal effect on most orally **administered drugs** and However, slowly absorbed orally **administered drugs** and rectally **administered drugs** may be subjected to substantial bacterial metabolism.
Habitat and diet play major roles in determining...347-390. J.P. Skelly, G.L. Amidon, W.H. Barr et. al., Pharm. Res. **7** , 975 (1990) P.G. Welling. Dosage Routes; Bioavailability and Clinical Efficacy. In Pharmacokinetics: Regulatory, Industrial...

...Kotzan, J.T. Stewart, W.J. Brown, V.P. Shah, and F.R. Pelsor, Biopharm, **Drug** Disp., **7** , 281-291 (1986). F. Lagenbucher and J. Myscika, Br. J. Clin. Pharmac., 19, 151S-162S...M.A. Walker, V.K. Prasad, J. Lin, G. Knapp and B.E. Cabana, Biopharm. **Drug** Disp. 5, 11-19 (1984). H. Ogata, N. Aoyagi. K. Kaniwa, T. Shibazaki, A. Ejima...

...Tox., 22(4), 175-183 (1984). R. B. Patel et al. J. Pharm. Sci., 73(**7**), 964-966 (1984). U.V. Banakar and L.H. Block, Pharm. Tech, **7** , 103, (1984). N. Kaniwa, H. Ogata, N. Aoyagi,T. Shibazaki, et al. Int. J. Clin...
...Toxicol., 21, 56-63 (1983). V.K. Prasad et al., Int.J. Pharm. 13, 1- **7** (1983). T.J. Goehl et al. Int. J. Pharm. 15, 115-123 (1983). F. Lagenbucher ...

...Moller, Pharm. Ind. 45,623, (1983). V.P. Shah et al., J. Pharm. Sci., 71(**7**), 822-824 (1982). H.M. von Hattinberg et al. In: Methods in Clinical Pharmacology, N...

...Pharm. Pharmac., 25, 968-973, (1973). G.L. Mattok et al. Can. J. Pharm. Sci., **7** , 84-87 (1972). G. Levy. Indus. Pharmacy Section Sym., APhA, Ann. Mtg. Dallas, TX (1966...

DESCRIPTORS: **Drug delivery** systems...
19930100

38/5,K/69 (Item 59 from file: 148)

04165913 SUPPLIER NUMBER: 08119625 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Pulmonary thromboembolism: guidelines for use of thrombolytic and anticoagulant therapy.

Wood, Richard G.; Kinasewitz, Gary T.

Consultant, v29, n10, p38(8)
Oct, 1989
ISSN: 0010-7069 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT
WORD COUNT: 3814 LINE COUNT: 00336

CAPTIONS: Anticoagulant activity of heparin. (chart); Decisions in treatment of patients with pulmonary embolism. (chart); Contraindications to medical treatment of pulmonary embolism. (table); Characteristics of thrombolytic agents. (table); Rate of recurrent thromboembolic events following discharge. (graph)

SPECIAL FEATURES: illustration; chart; table; graph
INDUSTRY CODES/NAMES: HLTH Healthcare
DESCRIPTORS: Anticoagulants (Medicine)--Physiological aspects; Pulmonary embolism--Drug therapy; Thrombolytic drugs--Physiological aspects; Thromboembolism--Drug therapy
SIC CODES: 8011 Offices & clinics of medical doctors
FILE SEGMENT: TI File 148

... patients with acute pulmonary thrombeoemolism. The vast majority of these patients can be treated for 7 to 10 days with intravenous heparin, followed by 3 months of out-patient oral **anticoagulation** therapy with warfarin. Those with massive embolism should receive **thrombolytic** therapy followed by conventional heparin treatment and subsequent outpatient **anticoagulation** . The complications of **anticoagulation** are recurrent thromboembolism and bleeding. Surgical intervention may be indicated if there is a contraindication to **anticoagulation** or when complications occur during **anticoagulant** therapy.

Acute pulmonary embolism is a common clinical entity that is directly responsible for the...

...dosage. Heparin can be administered subcutaneously, by intermittent IV bolus, or as a continuous IV **infusion** . After an initial loading bolus, continuous **infusion** provides reliable **anticoagulation** and has a low incidence of bleeding complications. The incidence of major bleeding associated with...

...probably related to the increased total daily dose of heparin required when using intermittent bolus **administration** to maintain an **anticoagulated** state.

Adequate **anticoagulation** is achieved when sufficient heparin is **administered** to prolong the activated partial thromboplastin time (aPTT) to 1.5 to 2.0 times the **infusion** to ensure that adequate, but not excessive, **anticoagulation** has been achieved. Once the heparin **infusion rate** has been stabilized, monitor the aPTT daily.

Complications. Serious bleeding is the major complication of...

...reserve in case of recurrent embolism.

Despite the fact that virtually complete resolution of the **perfusion** defects was observed in both the heparin and the **thrombolytic** groups of the UPET study, thrombolytic therapy may also have additional benefits. Compared with the...

...repeated use. Urokinase is, however, much more expensive than streptokinase (Table 2). Dosage of this **thrombolytic** agent is calculated according to body weight. It is **administered** as a continuous IV infusion for 12 hours, followed by conventional heparin **infusion** .

Table : Table 2 - Characteristics of **thrombolytic** agents

Features	Streptokinase	Urakinase	TPA
Half-life (min)	23	16	8
Dose	100,000 IU		

...incidence of recurrent

thromboembolism is highest during the first 12 weeks after the acute episode.[7] This rate can be reduced by maintaining patients on oral **anticoagulant** therapy for at least 3 months after they have completed 7 to 10 days of inhospital treatment for pulmonary embolism (Figure 2). After the first 12 weeks, you must weigh the risk of bleeding complications against the benefits of **anticoagulation** .

Warfarin, a member of the coumarin group, is an oral anticoagulant that acts by interfering...effect may be caused in part by the complex pathway of warfarin absorption and by **drug** interactions.

Subcutaneously **administered** heparin has been used in several studies as an alternative to warfarin after patients are...

...demonstrated significant reduction in the bleeding complication when compared with conventional warfarin therapy.[8]

Subcutaneously **administered** heparin provides an acceptable option for long-term **anticoagulation** in the pregnant patient (for whom warfarin is contraindicated), in the patient who is at...

...pulmonary embolism. N Engl J Med. 1973;289:55-58. [4.] Barritt DW, Jordan SC. **Anticoagulant drugs** in the treatment of pulmonary embolism: a controlled trial. Lancet. 1960;1:1309-1312. [5...
...6.] Kempezinski RF. Surgical prophylaxis of pulmonary embolism. Chest. 1986;89 (suppl 5); 384s-387s. [7 .] Coon WW, Willis PW. Recurrence of venous thromboemolism. Surgery. 1973;73:823-827. [8.] Hull...

19891000

38/5,K/103 (Item 26 from file: 444)
DIALOG(R)File 444:New England Journal of Med.

00104065

Intermittent Coronary Occlusion in Acute Myocardial Infarction: Value of Combined Thrombolytic and Vasodilator Therapy (Original Article)

Hackett, David, M.B.; M.R.C.P.I.; Davies, Graham, M.R.C.P.; Chierchia, Sergio; Maseri, Attilio, F.A.C.C.
The New England Journal of Medicine
October 22, **1987** ; 317 (17),pp 1055-1059
LINE COUNT: 00384 WORD COUNT: 05312
ISSN: 0028-4793

Abstract

We performed continuous electrocardiographic ST-segment monitoring and serial coronary arteriography in 45 consecutive patients presenting in the early stages of acute myocardial infarction. During cardiac catheterization, 28 episodes of arteriographically confirmed coronary reopening and subsequent reocclusion were observed in 16 patients before (3 episodes) and during (25 episodes) continuous intracoronary infusion of streptokinase. In addition, ST-segment monitoring demonstrated 12 episodes of spontaneous transient return of the ST segment to the base line in eight patients between the time of admission and the performance of coronary arteriography. During arteriographically documented reocclusion, intracoronary isosorbide dinitrate (2 mg) reestablished the patency of the coronary artery within one to two minutes in 14 of 28 episodes that occurred in 11 of 16 patients. After streptokinase infusion, intracoronary administration of isosorbide dinitrate was followed by dilatation of the infarct-related stenosis from a mean value (+/- SD) of 1.12 +/- 0.3 mm (58.1 +/- 12.1 percent) to 1.33 +/- 0.4 mm (51.6 +/- 12.9 percent; P = 0.004).

Spontaneous intermittent coronary recanalization and reocclusion resulting from a variable combination of thrombosis and vasoconstriction are frequent during the early phase of acute myocardial infarction. We propose that the combination of intracoronary streptokinase and isosorbide dinitrate may increase the rate of stable coronary recanalization. (N Engl

J Med 1987; 317:1055-9).

CITED REFERENCES

1. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront phenomenon of ischemic cell death. I. Myocardial infarct size vs duration of coronary occlusion in dogs. Circulation 1977; 56:786-94.
2. Maseri A, Chierchia S, Davies G. Pathophysiology of coronary occlusion in acute infarction. Circulation 1986; 73:233-9.
3. Davies GJ, Chierchia S, Maseri A. Prevention of myocardial infarction by very early treatment with intracoronary streptokinase: some clinical observations. N Engl J Med 1984; 311:1488-92.
4. Wagner GS, Freye CJ, Palmeri ST, et al. Evaluation of a QRS scoring system for estimating myocardial infarct size. I. Specificity and observer agreement. Circulation 1982; 65:342-7.
5. Gallino A, Chierchia S, Smith G, et al. Computer system for analysis of ST segment changes on 24 hour Holter monitor tapes: comparison with other available systems. J Am Coll Cardiol 1984; 4:245-52.
6. Morgan MJ, Croom M, Chierchia S, Maseri A. A flexible system for intelligent display of electrocardiographic, pressure and nuclear medicine data recorded over a period of several hours. Computers in Cardiology, Long Beach, Calif.: IEEE Computer Society, 1983:329-32.
7. The TIMI Study Group. The **thrombolysis** in myocardial infarction (TIMI) trial: Phase 1 findings. N Engl J Med 1985; 312:932-6.
8. Reiber JHC, Kooijman CJ, Slager CJ, et al. Computer assisted analysis of the severity of obstructions from coronary cineangiograms: a methodological review. Automedica 1984; 5:219-38.
9. Thygesen K, Horder M, Nielsen BL, Peterson PH. The variability of ST segment in the early phase of acute myocardial infarction. Acta Med Scand Suppl] 1979; 623:61-70.
10. Bren GB, Wasserman AG, Ross AM. Hazards of using post **thrombolytic** ST segment evolution as a reperfusion marker. J Am Coll Cardiol 1986; 7 :17A. abstract.
11. Laffel GL, Braunwald E. **Thrombolytic** therapy: a new strategy for the treatment of acute myocardial infarction. N Engl J Med 1984; 311:710- 7 , 770-6.
12. Yusuf S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction: overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. Eur Heart J 1985; 6:556-85.
13. DeWood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 1980; 303:897-902.
14. Rentrop KP, Feit F, Blanke H, et al. Effects of intracoronary streptokinase and intracoronary nitroglycerin infusion on coronary angiographic patterns and mortality in patients with acute myocardial infarction. N Engl J Med 1984; 311:1457-63.
15. Willerson JT, Hillis LD, Winniford M, Buja LM. Speculation regarding mechanisms responsible for acute ischemic heart disease syndromes. J Am Coll Cardiol 1986; 8:245-50.
16. Bush LR, Campbell WB, Buja LM, Tilton GD, Willerson JT. Effects of the selective thromboxane synthetase inhibitor dazoxiben on variations in cyclic blood flow in stenosed canine coronary arteries. Circulation 1984; 69:1161-70.
17. Schmitz JM, Apprill PG, Buja LM, Willerson JT, Campbell WB. Vascular prostaglandin and thromboxane production in a canine model of myocardial ischemia. Circ Res 1985; 57:223-31.
18. Hackett D, Larkin S, Chierchia S, Davies G, Kaski JC, Maseri A. Induction of coronary artery spasm by a direct local action of ergonovine. Circulation 1987; 75:577-82.
19. Maseri A. Role of coronary artery spasm in symptomatic and silent myocardial ischemia. J Am Coll Cardiol 1987; 9:249-62. □

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

1987 ;

TEXT

...was graded from 0 (complete occlusion) to 3 (patency), according to the criteria of the **Thrombolysis** in Myocardial Infarction (TIMI) Study Group,

(Ref. **7**) by two blinded observers; in the four cases in which disagreement occurred, it was resolved...2388 +/- 1508 IU per liter, P = 0.8), in Wagner QRS score (Ref. 4) before **thrombolysis** (2.43 +/- 2.1 vs. 2.38 +/- 2.1, P = 0.9) or after **thrombolysis** (5.95 +/- 4. **7** vs. 4.57 +/- 4.0, P = 0.3), or in the incidence of angiographically detected...in the size of the minimal residual diameter of the infarct-related coronary stenoses after **thrombolysis** between patients with intermittent occlusion (1.07 +/- 0.3 mm 61.3 +/- 11.0 percent...

...improvement following isosorbide dinitrate administration whenever the occlusion was incomplete. The failure of direct intracoronary **administration** of isosorbide dinitrate to induce coronary patency before **thrombolysis** does not necessarily imply that vasoconstriction does not have a role in acute infarction. Nitrates...

...laboratory animals (Ref. 16,17). At a later stage, when initial recanalization is achieved by **thrombolysis** , nitrates may become effective in relieving vasoconstriction because of their **delivery** in adequate concentrations to the relevant coronary segment. After **thrombolysis** , the increase in the caliber of the residual stenosis that follows another intracoronary dose of...infarction suggests that thrombolytic therapy may be complemented by high doses of selective intracoronary vasodilator **drugs** , which can increase the **flow rate** in subtotally occluded vessels and reopen vessels that become reoccluded during infusion of streptokinase. In turn, this increase in flow would be expected to result in better **delivery** of the **thrombolytic** agent along the thrombotic coronary segment.

CITED REFERENCES

...of several hours. Computers in Cardiology, Long Beach, Calif.: IEEE Computer Society, 1983:329-32.

7 . The TIMI Study Group. The **thrombolysis** in myocardial infarction (TIMI) trial: Phase 1 findings. N Engl J Med 1985; 312:932...

...1979; 623:61-70.

10. Bren GB, Wasserman AG, Ross AM. Hazards of using post **thrombolytic** ST segment evolution as a reperfusion marker. J Am Coll Cardiol 1986; **7** :17A. abstract.
11. Laffel GL, Braunwald E. **Thrombolytic** therapy: a new strategy for the treatment of acute myocardial infarction. N Engl J Med 1984; 311:710- **7** , 770-6.
12. Yusuf S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic...

38/5,K/106 (Item 29 from file: 444)

00103741

Intermittent Coronary Occlusion in Acute Myocardial Infarction: Value of Combined Thrombolytic and Vasodilator Therapy (Original Article)

Hackett, David, M.B., M.R.C.P.I.; Davies, Graham, M.R.C.P.; Chierchia, Sergio; Maseri, Attilio, F.A.C.C.

The New England Journal of Medicine
October 22, **1987** ; 317 (17),pp 1055-1059
LINE COUNT: 00384 WORD COUNT: 05312
ISSN: 0028-4793

Abstract

We performed continuous electrocardiographic ST-segment monitoring and serial coronary arteriography in 45 consecutive patients presenting in the early stages of acute myocardial infarction. During cardiac catheterization, 28 episodes of arteriographically confirmed coronary reopening and subsequent reocclusion were observed in 16 patients before (3 episodes) and during (25 episodes) continuous intracoronary infusion of streptokinase. In addition, ST-segment monitoring demonstrated 12 episodes

of spontaneous transient return of the ST segment to the base line in eight patients between the time of admission and the performance of coronary arteriography. During arteriographically documented reocclusion, intracoronary isosorbide dinitrate (2 mg) reestablished the patency of the coronary artery within one to two minutes in 14 of 28 episodes that occurred in 11 of 16 patients. After streptokinase infusion, intracoronary administration of isosorbide dinitrate was followed by dilatation of the infarct-related stenosis from a mean value (+/- SD) of 1.12 +/- 0.3 mm (58.1 +/- 12.1 percent) to 1.33 +/- 0.4 mm (51.6 +/- 12.9 percent; P = 0.004).

Spontaneous intermittent coronary recanalization and reocclusion resulting from a variable combination of thrombosis and vasoconstriction are frequent during the early phase of acute myocardial infarction. We propose that the combination of intracoronary streptokinase and isosorbide dinitrate may increase the rate of stable coronary recanalization. (N Engl J Med 1987; 317:1055-9).

CITED REFERENCES

1. Reimer KA, Lowe JE, Rasmussen MM, Jennings RB. The wavefront phenomenon of ischemic cell death. I. Myocardial infarct size vs duration of coronary occlusion in dogs. Circulation 1977; 56:786-94.
2. Maseri A, Chierchia S, Davies G. Pathophysiology of coronary occlusion in acute infarction. Circulation 1986; 73:233-9.
3. Davies GJ, Chierchia S, Maseri A. Prevention of myocardial infarction by very early treatment with intracoronary streptokinase: some clinical observations. N Engl J Med 1984; 311:1488-92.
4. Wagner GS, Freye CJ, Palmeri ST, et al. Evaluation of a QRS scoring system for estimating myocardial infarct size. I. Specificity and observer agreement. Circulation 1982; 65:342-7.
5. Gallino A, Chierchia S, Smith G, et al. Computer system for analysis of ST segment changes on 24 hour Holter monitor tapes: comparison with other available systems. J Am Coll Cardiol 1984; 4:245-52.
6. Morgan MJ, Croom M, Chierchia S, Maseri A. A flexible system for intelligent display of electrocardiographic, pressure and nuclear medicine data recorded over a period of several hours. Computers in Cardiology, Long Beach, Calif.: IEEE Computer Society, 1983:329-32.
7. The TIMI Study Group. The **thrombolysis** in myocardial infarction (TIMI) trial: Phase 1 findings. N Engl J Med 1985; 312:932-6.
8. Reiber JHC, Kooijman CJ, Slager CJ, et al. Computer assisted analysis of the severity of obstructions from coronary cineangiograms: a methodological review. Automedica 1984; 5:219-38.
9. Thygesen K, Horder M, Nielsen BL, Peterson PH. The variability of ST segment in the early phase of acute myocardial infarction. Acta Med Scand Suppl] 1979; 623:61-70.
10. Bren GB, Wasserman AG, Ross AM. Hazards of using post **thrombolytic** ST segment evolution as a reperfusion marker. J Am Coll Cardiol 1986; **7** :17A. abstract.
11. Laffel GL, Braunwald E. **Thrombolytic** therapy: a new strategy for the treatment of acute myocardial infarction. N Engl J Med 1984; 311:710- **7** , 770-6.
12. Yusuf S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction: overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. Eur Heart J 1985; 6:556-85.
13. DeWood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 1980; 303:897-902.
14. Rentrop KP, Feit F, Blanke H, et al. Effects of intracoronary streptokinase and intracoronary nitroglycerin infusion on coronary angiographic patterns and mortality in patients with acute myocardial infarction. N Engl J Med 1984; 311:1457-63.
15. Willerson JT, Hillis LD, Winniford M, Buja LM. Speculation regarding mechanisms responsible for acute ischemic heart disease syndromes. J Am Coll Cardiol 1986; 8:245-50.
16. Bush LR, Campbell WB, Buja LM, Tilton GD, Willerson JT. Effects of the selective thromboxane synthetase inhibitor dazoxiben on variations in cyclic blood flow in stenosed canine coronary arteries. Circulation 1984; 69:1161-70.

17. Schmitz JM, Apprill PG, Buja LM, Willerson JT, Campbell WB. Vascular prostaglandin and thromboxane production in a canine model of myocardial ischemia. Circ Res 1985; 57:223-31.
18. Hackett D, Larkin S, Chierchia S, Davies G, Kaski JC, Maseri A. Induction of coronary artery spasm by a direct local action of ergonovine. Circulation 1987; 75:577-82.
19. Maseri A. Role of coronary artery spasm in symptomatic and silent myocardial ischemia. J Am Coll Cardiol 1987; 9:249-62. □

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

1987 ;

TEXT

...was graded from 0 (complete occlusion) to 3 (patency), according to the criteria of the **Thrombolysis** in Myocardial Infarction (TIMI) Study Group, (Ref. **7**) by two blinded observers; in the four cases in which disagreement occurred, it was resolved...2388 +/- 1508 IU per liter, P = 0.8), in Wagner QRS score (Ref. 4) before **thrombolysis** (2.43 +/- 2.1 vs. 2.38 +/- 2.1, P = 0.9) or after **thrombolysis** (5.95 +/- 4. **7** vs. 4.57 +/- 4.0, P = 0.3), or in the incidence of angiographically detected...in the size of the minimal residual diameter of the infarct-related coronary stenoses after **thrombolysis** between patients with intermittent occlusion (1.07 +/- 0.3 mm 61.3 +/- 11.0 percent...

...improvement following isosorbide dinitrate administration whenever the occlusion was incomplete. The failure of direct intracoronary **administration** of isosorbide dinitrate to induce coronary patency before **thrombolysis** does not necessarily imply that vasoconstriction does not have a role in acute infarction. Nitrates...

...laboratory animals (Ref. 16,17). At a later stage, when initial recanalization is achieved by **thrombolysis** , nitrates may become effective in relieving vasoconstriction because of their **delivery** in adequate concentrations to the relevant coronary segment. After **thrombolysis** , the increase in the caliber of the residual stenosis that follows another intracoronary dose of...infarction suggests that thrombolytic therapy may be complemented by high doses of selective intracoronary vasodilator **drugs** , which can increase the **flow rate** in subtotally occluded vessels and reopen vessels that become reoccluded during infusion of streptokinase. In turn, this increase in flow would be expected to result in better **delivery** of the **thrombolytic** agent along the thrombotic coronary segment.

CITED REFERENCES

...of several hours. Computers in Cardiology, Long Beach, Calif.: IEEE Computer Society, 1983:329-32.
7 . The TIMI Study Group. The **thrombolysis** in myocardial infarction (TIMI) trial: Phase 1 findings. N Engl J Med 1985; 312:932...

...1979; 623:61-70.
10. Bren GB, Wasserman AG, Ross AM. Hazards of using post **thrombolytic** ST segment evolution as a reperfusion marker. J Am Coll Cardiol 1986; **7** :17A. abstract.
11. Laffel GL, Braunwald E. **Thrombolytic** therapy: a new strategy for the treatment of acute myocardial infarction. N Engl J Med 1984; 311:710- **7** , 770-6.
12. Yusuf S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic...

38/5,K/110 (Item 33 from file: 444)

00102421

Continuous Intravenous Heparin Compared with Intermittent Subcutaneous Heparin in the Initial Treatment of Proximal-Vein Thrombosis (Original Article)

Hull, Russell D., M.B.B.S., M.Sc.; Raskob, Gary E., M.Sc.; Hirsh, Jack; Jay, Richard M.; Leclerc, Jacques R.; Geerts, William H.; Rosenbloom, David, Pharm.D.; Sackett, David L.; Anderson, Christine, R.N.; Harrison, Linda, R.N.; Gent, Michael, M.Sc.
The New England Journal of Medicine
October 30, **1986** ; 315 (18),pp 1109-1114
LINE COUNT: 00509 WORD COUNT: 07030
ISSN: 0028-4793

Abstract

We performed a randomized double-blind trial comparing continuous intravenous heparin with intermittent subcutaneous heparin in the initial treatment of 115 patients with acute proximal deep-vein thrombosis. Intermittent subcutaneous heparin as administered in this trial was inferior to continuous intravenous heparin in preventing recurrent venous thromboembolism. The subcutaneous heparin regimen induced an initial anticoagulant response below the target therapeutic range in the majority of patients and resulted in a high frequency of recurrent venous thromboembolism (11 of 57 patients, 19.3 percent), which was virtually confined to patients with a subtherapeutic anticoagulant response. In contrast, continuous intravenous heparin induced a therapeutic anticoagulant response in the majority of patients and a low frequency of recurrent events (3 of 58 patients, 5.2 percent; P = 0.024); the recurrences were limited to patients with an initial subtherapeutic anticoagulant response.

The results of this trial establish the efficacy of intravenous heparin in the treatment of proximal venous thrombosis and suggest a relation between the effectiveness of heparin and the levels of anticoagulation achieved; such a relation could explain the observed failure of the subcutaneous regimen. (N Engl J Med 1986; 315:1109-14).

CITED REFERENCES

1. Deykin D. Anticoagulant therapy. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. Hemostasis and thrombosis: basic principles and clinical practice. Philadelphia: JB Lippincott, 1982:1000-12.
2. Moser KM. Pulmonary thromboembolism. In: Petersdorf RG, Adams RD, Braunwald E, Isselbacher KJ, Martin JB, Wilson JD, eds. Harrison's principles of internal medicine. 10th ed. New York: McGraw-Hill, 1983:1561-7.
3. Wessler S, Gitel S. Control of heparin therapy. Prog Hemost Thromb 1976; 3:311-29.
4. Wessler S, Gitel SN. Heparin: new concepts relevant to clinical use. Blood 1979; 53:525-44.
5. Marder VJ. Variations of heparin therapy for thromboembolic disease. Med Clin North Am 1974; 58:1121-8.
6. Gurewich V. Guidelines for the management of anticoagulant therapy. Semin Thromb Hemost 1976; 2:176-96.
7. Salzman EW, Deykin D, Shapiro RM, Rosenberg R. Management of heparin therapy: controlled prospective trial. N Engl J Med 1975; 292:1046-50.
8. Glazier RL, Crowell EB. Randomized prospective trial of continuous vs intermittent heparin therapy. JAMA 1976; 236:1365-7.
9. Mant MJ, O'Brien BD, Thong KL, Hammond GW, Birtwhistle RV, Grace MG. Hemorrhagic complications of heparin therapy. Lancet 1977; 1:1133-5.
10. Wilson JR, Lampman J. Heparin therapy: a randomized prospective study. Am Heart J 1979; 97:155-9.
11. Hull R, Delmore T, Genton E, et al. Warfarin sodium versus low-dose heparin in the long-term treatment of venous thrombosis. N Engl J Med 1979; 301:855-8.
12. Hull R, Delmore T, Carter C, et al. Adjusted subcutaneous heparin versus warfarin sodium in the long-term treatment of venous thrombosis. N Engl J Med 1982; 306:189-94.
13. Hull R, Hirsh J, Jay R, et al. Different intensities of oral anticoagulant therapy in the treatment of proximal-vein thrombosis. N Engl J Med 1982; 307:1676-81.
14. Andersson G, Fagrell B, Holmgren K, et al. Subcutaneous administration of heparin: a randomised comparison with intravenous administration of heparin to patients with deep-vein thrombosis. Thromb Res 1982;

27:631-9.
15. Yin ET, Wessler S, Butler JV. Plasma heparin: a unique, practical submicrogram-sensitive assay. J Lab Clin Med 1973; 81:298-310.
16. Rabinov K, Paulin S. Roentgen diagnosis of venous thrombosis in the leg. Arch Surg 1972; 104:134-44.
17. Hull R, Hirsh J, Sackett DL, Powers P, Turpie AGG, Walker I. Combined use of leg scanning and impedance plethysmography in suspected venous thrombosis: an alternative to venography. N Engl J Med 1977; 296:1497-500.
18. Sackett DL. Bias in analytic research. J Chronic Dis 1979; 32:51-63.
19. Refn I, Raaschou F, Vestergaard L. Subcutaneous application of heparin. In: Koller T, Merz WR, eds. Thrombosis and embolism: proceedings of the International Conference. Basel: Benno Schwabe & Co., 1954:758-62.
20. Griffith GC, Boggs RP. The clinical usage of heparin. Am J Cardiol 1964; 14:39-46.
21. Hirsh J, O'Sullivan EF, Gallus AS, Martin M. Evaluation of subcutaneous calcium heparin therapy in the treatment of thrombo-embolic disease. Med J Aust 1970; 1:15-7.
22. Raskob GE, Hull RD, LeClerc JR, et al. Sustained therapeutic heparinization by subcutaneous administration for the primary treatment of acute venous thrombosis. Circulation 1984; 70:Suppl 2:II-360.
23. Hull RD, Carter CJ, Jay RM, et al. The diagnosis of acute, recurrent, deep-vein thrombosis: a diagnostic challenge. Circulation 1983; 67:901-6. 24. Hull RD, Hirsh J, Carter CJ, et al. Diagnostic value of ventilation-perfusion lung scanning in patients with suspected pulmonary embolism. Chest 1985; 88:819-28.
25. McNeil BJ. Ventilation-perfusion studies and the diagnosis of pulmonary embolism: concise communication. J Nucl Med 1980; 21:319-23.
26. Biello DR, Mattar AG, McKnight RC, Siegel BA. Ventilation-perfusion studies in suspected pulmonary embolism. AJR 1979; 133:1033-7.
27. Refn I, Vestergaard L. The titration of heparin with protamine. Scand J Clin Lab Invest 1954; 6:284-7.
28. Holmgren K, Andersson G, Fagrell B, et al. One-month versus six-month therapy with oral anticoagulants after symptomatic deep-vein thrombosis. Acta Med Scand 1985; 218:279-84.
29. Schulman S, Lockner D. Relationship between thromboembolic complications and intensity of treatment during long-term prophylaxis with oral anticoagulants following DVT. Thromb Hemost 1985; 53:137-40.
30. Basu D, Gallus A, Hirsh J, Cade J. A prospective study of the value of monitoring heparin treatment with the activated partial thromboplastin time. N Engl J Med 1972; 287:324-7. □

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

1986 ;

TEXT

...trials have recently demonstrated that it is necessary to follow heparin treatment with long-term **anticoagulant** therapy in patients with proximal-vein thrombosis, to protect against recurrent venous thromboembolism (Ref. 11...

...1) and an interpretation awaits further clinical trials, as do conclusions about the intensity (Ref. 7) of heparinization required to prevent recurrent venous thromboembembolism...to avoid unblinding on the basis of knowledge of heparin clearance, all dose adjustments and **anticoagulant** monitoring in both groups were based on this daily mid-interval measurement. The mid-interval...
...range is achieved, the mid-interval activated partial thromboplastin time predicts a sustained and therapeutic **anticoagulant** response throughout the 12-hour period between **injections** (Ref. 12,22). Both heparin regimens were adjusted daily to maintain the activated partial thromboplastin...

...a dosage schedule established before the trial. Changes were implemented simultaneously in both the intravenous **infusion rate** and the subcutaneous injection volume in every patient, keeping changes in total 24-hour heparin...0.001). All but one of the recurrences were in patients with an inadequate initial **anticoagulant** response. Thus, the episodes of

recurrent venous thromboembolism observed in this trial were associated with, and probably the result of, an inadequate **anticoagulant** response (Fig. 1 and Table 4). This conclusion is supported by the additional observation that the relative risk of recurrent venous thromboembolism was 15 times higher in patients with inadequate **anticoagulation** during the first 24 hours or more (13 of 53 patients, 24.5 percent) than in patients with an **anticoagulant** response in the prescribed therapeutic range (1 of 62 patients, 1.6 percent; P<0...

...On day 1 the mean values in the subcutaneously and intravenously treated groups were 57. **7** and 73.4 seconds, respectively, in patients without recurrent venous thromboembolism (P = 0.002) and...

...and the optimal therapeutic range have been subjects of debate for many years (Ref. 1- **7**). An uncontrolled prospective study (Ref. 30) has suggested that recurrent venous thromboembolism is infrequent if...

...Our findings, based on a controlled trial of two heparin regimens that produced significantly different **anticoagulant** responses early in the course of therapy, provide evidence of the need for an adequately intense heparin effect and support this clinical practice. Inadequate **anticoagulant** therapy clearly places patients with proximal-vein thrombosis at considerable risk of serious morbidity and...
?
?